Music interventions for mechanically ventilated patients (Review)

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T A B L E   O F   C O N T E N T S

[Intervention Review]

Music interventions for mechanically ventilated patients

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ABSTRACT

Background

Mechanical ventilation often causes major distress and anxiety in patients. The sensation of breathlessness, frequent suctioning, inability to talk, uncertainty regarding surroundings or condition, discomfort, isolation from others, and fear contribute to high levels of anxiety. Side effects of analgesia and sedation may lead to the prolongation of mechanical ventilation and, subsequently, to a longer length of hospitalization and increased cost. Therefore, non-pharmacological interventions should be considered for anxiety and stress management. Music interventions have been used to reduce anxiety and distress and improve physiological functioning in medical patients; however, their efficacy for mechanically ventilated patients needs to be evaluated. This review was originally published in 2010 and was updated in 2014.

Objectives

To update the previously published review that examined the effects of music therapy or music medicine interventions (as defined by the authors) on anxiety and other outcomes in mechanically ventilated patients. Specifically, the following objectives are addressed in this review.

1. To conduct a meta-analysis to compare the effects of participation in standard care combined with music therapy or music medicine interventions with standard care alone.

2. To compare the effects of patient-selected music with researcher-selected music.

3. To compare the effects of different types of music interventions (e.g., music therapy versus music medicine).

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2014, Issue 2), MEDLINE (1950 to March 2014), CINAHL (1980 to March 2014), EMBASE (1980 to March 2014), PsycINFO (1967 to March 2014), LILACS (1982 to March 2014), Science Citation Index (1980 to March 2014), www.musictherapyworld.net (1 March 2008) (database is no longer functional), CAIRSS for Music (to March 2014), Proquest Digital Dissertations (1980 to March 2014), ClinicalTrials.gov (2000 to March 2014), Current Controlled Trials (1998 to March 2014), the National Research Register (2000 to September 2007), and NIH CRISP (all to March 2014). We handsearched music therapy journals and reference lists, and contacted relevant experts to identify unpublished manuscripts. There was no language restriction. The original search was performed in January 2010.

Selection criteria

We included all randomized and quasi-randomized controlled trials that compared music interventions and standard care with standard care alone for mechanically ventilated patients.

Data collection and analysis

Two review authors independently extracted the data and assessed the methodological quality of included studies. We contacted authors to obtain missing data where needed. Where possible, results for continuous outcomes were presented in meta-analyses using mean differences and standardized mean differences. Post-test scores were used. In cases of significant baseline difference, we used change scores. For dichotomous outcomes, we presented the results as risk ratios.

Main results

We identified six new trials for this update. In total, the evidence for this review rests on 14 trials (805 participants). Music listening was the main intervention used, and 13 of the studies did not include a trained music therapist. Results indicated that music listening may be beneficial for anxiety reduction in mechanically ventilated patients. Specifically, music listening resulted, on average, in an anxiety reduction that was 1.11 standard deviation units greater (95% CI -1.75 to -0.47, P = 0.0006) than in the standard care group. This is considered a large and clinically significant effect. Findings indicated that listening to music consistently reduced respiratory rate and systolic blood pressure, suggesting a relaxation response. Furthermore, one large-scale study reported greater reductions in sedative and analgesic intake in the music listening group compared to the control group, and two other studies reported trends for reduction in sedative and analgesic intake for the music group. One study found significantly higher sedation scores in the music listening group compared to the control group.

No strong evidence was found for reduction in diastolic blood pressure and mean arterial pressure. Furthermore, inconsistent results were found for reduction in heart rate with seven studies reporting greater heart rate reductions in the music listening group and one study a slightly greater reduction in the control group. Music listening did not improve oxygen saturation levels.

Four studies examined the effects of music listening on hormone levels but the results were mixed and no conclusions could be drawn.

No strong evidence was found for an effect of music listening on mortality rate but this evidence rested on only two trials.

Most trials were assessed to be at high risk of bias because of lack of blinding. Blinding of outcome assessors is often impossible in music therapy and music medicine studies that use subjective outcomes, unless the music intervention is compared to another treatment intervention. Because of the high risk of bias, these results need to be interpreted with caution.

No studies could be found that examined the effects of music interventions on quality of life, patient satisfaction, post-discharge outcomes, or cost-effectiveness. No adverse events were identified.

Authors' conclusions

This updated systematic review indicates that music listening may have a beneficial effect on anxiety in mechanically ventilated patients. These findings are consistent with the findings of three other Cochrane systematic reviews on the use of music interventions for anxiety reduction in medical patients. The review furthermore suggests that music listening consistently reduces respiratory rate and systolic blood pressure. Finally, results indicate a possible beneficial impact on the consumption of sedatives and analgesics. Therefore, we conclude that music interventions may provide a viable anxiety management option to mechanically ventilated patients.

PLAIN LANGUAGE SUMMARY

Music interventions for mechanically ventilated patients

Review question

We reviewed the evidence on the effect of music interventions compared to standard care on anxiety and other outcomes in mechanically ventilated patients.

Background

Mechanical ventilation often causes major distress and anxiety in patients, putting them at greater risk for complications. Side effects of analgesia and sedation may lead to the prolongation of mechanical ventilation and, subsequently, to a longer length of hospitalization and increased cost. Therefore, non-pharmacological interventions should be considered for anxiety and stress management. Several studies have examined the impact of music interventions on anxiety and physiological responses in mechanically ventilated patients. Music interventions are categorized as 'music medicine' when passive listening to pre-recorded music is offered by medical personnel. In contrast, music therapy requires the implementation of a music intervention by a trained music therapist, the presence of a therapeutic process, and the use of personally tailored music experiences. A systematic review was needed to gauge the efficacy of both music therapy and music medicine interventions.

Search date

The evidence is current to March 2014.

Study characteristics

We included 14 controlled trials involving 805 critically ill participants on mechanical ventilation. All participants were alert. Slightly more patients (58%) included in these studies were male and their average age was 58 years.

The majority of the studies examined the effects of patients listening to pre-recorded music. Most studies offered one 20 to 30-minute music session to the participants.

Key results

The findings suggest that music listening may have a large anxiety-reducing effect on mechanically ventilated patients. The results furthermore suggest that music listening consistently reduces respiratory rate and systolic blood pressure, suggesting a relaxation response. No evidence of effect was found for diastolic blood pressure, mean arterial pressure, or oxygen saturation level and inconsistent results were found for heart rate and hormone levels. One large-scale study reported greater reductions in the intake of sedative and analgesic medications in the music listening group compared to the control group, and two other studies reported similar trends.

Music listening did not result in any harm.

Quality of the evidence

Most trials presented some methodological weakness. Therefore, these results need to be interpreted with caution. However, the results are consistent with the findings of three other Cochrane systematic reviews on the use of music interventions for anxiety reduction in medical patients. Therefore, we conclude that music interventions may provide a viable anxiety management option to mechanically ventilated patients.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Music compared to standard care for mechanically ventilated patients			
Patient or population: mechanically ventilated patients **Settings:** intensive care units **Intervention:** music **Comparison:** standard care			
Outcomes	**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**
State anxiety STAI, VAS	The mean state anxiety in the intervention groups was **1.11 standard deviations lower** (1.75 to 0.47 lower)	288 (5 studies)	⊕⊕○○ **low**[1,2,3,4]
Heart rate beats per minute	The mean heart rate in the intervention groups was **3.95 lower** (6.62 to 1.27 lower)	338 (8 studies)	⊕○○○ **very low**[1,5,6]
Respiratory rate breaths per minute	The mean respiratory rate in the intervention groups was **2.87 lower** (3.64 to 2.10 lower)	357 (9 studies)	⊕○○○ **very low**[1,6]
Systolic blood pressure mmHg	The mean systolic blood pressure in the intervention groups was **4.22 lower** (6.38 to 2.06 lower)	269 (6 studies)	⊕○○○ **very low**[1,7]
Diastolic blood pressure mmHg	The mean diastolic blood pressure in the intervention groups was **2.16 lower** (4.4 lower to 0.07 higher)	269 (6 studies)	⊕○○○ **very low**[1,7]
Mean arterial pressure mmHg	The mean arterial pressure in the intervention groups was **1.79 lower** (4.56 lower to 0.99 higher)	98 (3 studies)	⊕○○○ **very low**[1,7]
Oxygen saturation level	The mean oxygen saturation level in the intervention groups was **0.05 lower** (0.67 lower to 0.57 higher)	193 (4 studies)	⊕⊕○○ **low**[1]

CI: Confidence interval

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

[1] The majority of the trials were assessed as high risk of bias studies
[2] All point estimates favour music although the magnitude of the effect differs across studies
[3] Wide confidence interval, however, this is due to the fact that some studies reported very large beneficial effects of music on anxiety
[4] Large reduction in anxiety as evidenced by SMD of 1.11
[5] Results were inconsistent across studies as evidenced by $I^2 = 62\%$
[6] Somewhat wide confidence interval
[7] Wide confidence interval

B A C K G R O U N D

Description of the condition

Mechanical ventilation often causes major distress and anxiety in patients. The sensation of breathlessness, frequent suctioning, inability to talk, uncertainty regarding surroundings or condition, discomfort, isolation from others, and fear contribute to high levels of anxiety (Lindgren 2005; Wong 2001). Increased anxiety may in turn lead to breathing difficulty and greater distress during weaning attempts, that is, the process of liberating the patient from mechanical support and from the tracheal tube (Boles 2007; Lindgren 2005). Moreover, mechanically ventilated patients often experience adverse events, including constriction of arteries and the airways in the lungs, caused by this anxiety (Ledingham 1988). Therefore, analgesia and sedation are considered important in the management of patients who require mechanical ventilation.
Complications related to the use of analgesic and sedative agents are common, however, and the immobility resulting from sedation may contribute to venous thrombosis or pressure damage to the nerves and skin. Furthermore, immune responses may be weakened from extensive use of sedative medications (Suter 2002). These side effects may lead to the prolongation of mechanical ventilation and, subsequently, to a longer length of hospitalization and increased costs (Bobek 2001; Egerod 2002; Kollef 1998). Additionally, an increase in morbidity and mortality has been found in anxious, critically ill patients (Moser 1996).

Description of the intervention

A review of the literature on treatment interventions for mechanically ventilated patients (Thomas 2003) indicated that the four most frequently perceived stressors for mechanically ventilated patients are dyspnoea or difficulty breathing, anxiety, fear, and pain. Few non-pharmacological interventional studies looking at ways to reduce these stressors were found. Four interventions, that is, hypnosis and relaxation, patient education and information sharing, music therapy, and supportive touch have been investigated and results indicate that they may be helpful in reducing patient stress (Thomas 2003).
Music has been used in different medical fields to meet physiological, psychological, and spiritual needs of adult and paediatric patients. Research on the effects of music or music therapy for medical patients has burgeoned during the past 20 years and has included a variety of outcome measures in a wide range of specialty areas (Dileo 2005). Specifically, the anxiolytic effects of music have been studied in a variety of medical patients including surgical (Bradt 2013a; Bringman 2009; Koch 1998; Mok 2003), cardiac (Bradt 2013b; Hamel 2001; Mandel 2007; White 1999), and oncology (Bradt 2011; Bufalini 2009; Nguyen 2010) patients.
It is important to make a clear distinction between music interventions administered by medical or healthcare professionals (music medicine) and those implemented by trained music therapists (music therapy). A substantive set of data (Dileo 2005) indicates that music therapy interventions with medical patient populations are significantly more effective than music medicine inter-

ventions for a wide variety of outcomes. This difference might be attributed to the fact that music therapists individualize their interventions to meet patients' specific needs; more actively engage the patients in the music making; and employ a systematic therapeutic process, including assessment, treatment, and evaluation. As defined by Dileo (Dileo 1999), interventions are categorized as music medicine when listening to pre-recorded music is offered by medical personnel or is self-administered by the patient. In contrast, music therapy requires the implementation of a music intervention by a trained music therapist, the presence of a therapeutic process, and the use of personally tailored music experiences. These music experiences include:

1. listening to live, improvised, or pre-recorded music;
2. performing music on an instrument;
3. improvising music spontaneously using voice or instruments, or both;
4. composing music; and
5. music combined with other modalities (e.g., movement, imagery, art) (Dileo 2007).

Heiderscheit and colleagues (Heiderscheit 2011) point out that music listening as a self-administered intervention (that is with minimal or no assistance from a music therapist) can play an important role in the self-management of anxiety and distress in intensive care unit (ICU) environments. They emphasize that this type of music intervention can "empower a patient to utilize the music whenever they may need it and as often as they need it. This type of non-pharmacological and patient-directed approach gives the patient options to manage their symptoms even when a music therapist is not present or available" (Heiderscheit 2011 pp. 2-3). This might be of particular importance to adolescent patients. Given that adolescents, on average, listen to music 2.5 hours per day (Rideout 2005), continued use of music listening during mechanical ventilation may be especially effective in providing them with a sense of safety, control, and normalcy. Ghetti (Ghetti 2013) furthermore advocates for the use of live music, in contrast to pre-recorded music, with children and adolescents in paediatric ICUs as it allows for "the therapist to remain responsive to the changing needs of the child and family, to provide emotional support in real-time, to improvise lyrics based on the surroundings, and to incorporate family members into the provision of music".

A major advantage of listening to pre-recorded or live music for patients who are mechanically ventilated is that it does not require focused concentration or sustained energy levels (Chlan 2009).

Patients should select music they prefer since unfamiliar music or music disliked by the patient could increase anxiety and agitation (Heiderscheit 2011). In the case of mechanically ventilated patients, assessment of music preference may be challenging. Therefore, assessment of music preferences by a trained music therapist is recommended (Chlan 2009; Heiderscheit 2011). A music assessment intervention tool (MAT) for this purpose and guidelines for implementation have been published (Chlan 2009).

How the intervention might work

As outlined by Bradt and colleagues (Bradt 2013a), a common theory regarding the anxiety-reducing effects of music is that music can help patients focus their attention away from stressful events to something pleasant and soothing (Mitchell 2003; Nilsson 2008). Even though this is an important mechanism in anxiety reduction, it is important to emphasize that music does more than refocusing patients' attention. It provides the patient with an aesthetic experience that can offer comfort and peace during times of distress. In music interventions provided by a trained music therapist, the music therapist furthermore adapts the live music interactions to the in-the-moment needs of the patients. This often provides a deeply humanizing and validating experience for the patient. In addition, listening to self-selected pre-recorded music, initiated by the patient him or herself, may result in an increased sense of control and empowerment in a critical care environment where most aspects of care are beyond the patient's control (Chlan 2013).

On a neurophysiological level, it has been postulated that music induces relaxation through its impact on automated and central nervous responses (Beaulieu-Boire 2013; Gillen 2008; Lai 2006). More specifically, it is believed that the anxiolytic or anxiety-reducing effect of music is achieved through its suppressive action on the sympathetic nervous system, leading to decreased adrenergic activity (that is, reduced release of the stress hormone adrenaline) and decreased stimulation of nerves and muscles (Chlan 1998; Gillen 2008). Music furthermore triggers the limbic system, a section of the brain that plays an important role in the regulation of emotional responses, to release endorphins; these neurotransmitters play an important role in enhancing a sense of well-being (Arslan 2008; Beaulieu-Boire 2013). However, Gillen (Gillen 2008) has suggested that more research is needed to examine the physiological mechanisms that explain the anxiolytic effects of music.

It is important to note that there are a number of individual factors that may influence responses to music. These include, but are not limited to, age, gender, cognitive function, severity of stress, anxiety, discomfort and pain, training in music, familiarity with and preference for the music, culture, and personal associations with the music (Pelletier 2004; Standley 1986; Standley 2000). Music also evokes various types of imagery in many individuals. Thus, the individual's unique imagery experience will influence his or her responses to the music. Therefore, it cannot be assumed that sedative music will always have positive effects on individuals; careful monitoring of individual effects is needed.

Why it is important to do this review

Several research studies on the effects of music on mechanically ventilated patients have reported positive results. A number of these studies, however, have suffered from small sample size (Almerud 2003; Besel 2006; Chlan 1995; Wong 2001). In addition, differences in factors such as study design, methods of intervention, and types of music have led to varying results. A systematic review is needed to more accurately gauge the efficacy of music medicine or music therapy as anxiety-reducing interventions for mechanically ventilated patients, as well as to identify variables that may moderate the effects.

OBJECTIVES

To update the previously published review that examined the effects of music therapy or music medicine interventions (as defined by the authors) on anxiety and other outcomes in mechanically ventilated patients. Specifically, the following objectives are addressed in this review.

1. To conduct a meta-analysis to compare the effects of participation in standard care combined with music therapy or music medicine interventions with standard care alone.

2. To compare the effects of patient-selected music with researcher-selected music.

3. To compare the effects of different types of music interventions (e.g., music therapy versus music medicine).

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomized controlled trials (RCT) and controlled clinical trials (CCTs) with quasi-randomized or systematic methods of treatment allocation in any language, published and unpublished.

Types of participants

The review included studies of mechanically ventilated patients in an intensive or critical care unit, long term acute care hospital (LCAT), or 'step-down' unit. We imposed no restrictions as to age, gender, or ethnicity. We included both patients undergoing ventilation and patients who were being weaned after prolonged mechanical ventilation. The most frequently used modes of ventilatory support included synchronized intermittent mandatory ventilation and a pressure support mode. Types of airway management included oral endotracheal tube, nasal endotracheal tube, and tracheostomy tube.

Types of interventions

We included all studies in which standard treatment combined with music therapy or music medicine interventions (as defined by the authors) were compared with:

1. standard care alone;
2. standard care combined with other therapies; or
3. standard care with placebo. Placebo treatment involved the use of headphones for the patients wherein no music stimuli were provided or another type of auditory stimulus was provided (e.g., white noise (hiss), pink noise (sound of ocean waves), or nature sounds).

Types of outcome measures

Primary outcomes

1. State anxiety (defined as a temporary unpleasant emotional arousal in the face of threatening demands or dangers; this is in contrast with trait anxiety, which reflects the existence of stable individual differences in reactions (Spielberger 1983)), as reported by the study authors

Secondary outcomes

1. Sedative drug intake, as reported by the study authors
2. Physiological outcomes (e.g., heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate, oxygen saturation, airway pressure)
3. Quality of life, as reported by the study authors
4. Patient satisfaction, as reported by the study authors
5. Post-discharge patient outcomes (e.g., functional status, post-discharge quality of life), as reported by the study authors
6. Mortality
7. Cost-effectiveness

Search methods for identification of studies

Electronic searches

We used the search strategy for MEDLINE as was listed in the protocol (Appendix 1) and adapted it for the other databases. We updated the previously run searches from 2010 (Appendix 16). We searched the following electronic databases and trials registers:

1. Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2014, Issue 2);
2. MEDLINE (1966 to March 2014);
3. EMBASE (1980 to March 2014);
4. CINAHL (1982 to March 2014);
5. PsycINFO (1967 to March 2014);
6. LILACS (1982 to March 2014);

7. AMED (1985 to January 2010) (we no longer had access to AMED after this date);
8. Science Citation Index (1980 to March 2014);
9. the specialist music therapy research database at www.musictherapyworld.net (database is no longer functional) (1 March 2008);
10. CAIRSS for Music (March 2014);
11. Proquest Digital Dissertations (1980 to March 2014);
12. ClinicalTrials.gov (www.clinicaltrials.gov/) (2000 to March 2014);
13. Current Controlled Trials (www.controlled-trials.com/) (1998 to March 2014);
14. National Research Register at http://www.nihr.ac.uk/Pages/NRRArchive.aspx (2000 to September 2007) (register is no longer maintained);
15. NIH CRISP (March 2014).

The original search was performed in January 2010 (Bradt 2010).

Searching other resources

We handsearched the following journals, from the first available date:

1. *Australian Journal of Music Therapy* (March 2014);
2. *Canadian Journal of Music Therapy* (March 2014);
3. *The International Journal of the Arts in Medicine* (December 2007, latest issue was published in 1999);
4. *Journal of Music Therapy* (March 2014);
5. *Musik-, Tanz-, und Kunsttherapie* (Journal for Art Therapies in Education, Welfare and Health Care) (March 2014, latest issue available online 2013(1));
6. *Musiktherapeutische Umschau* (March 2014);
7. *Music Therapy* (December 2007, latest issue published in 1996);
8. *Music Therapy Perspectives* (March 2014);
9. *Nordic Journal of Music Therapy* (March 2014);
10. *Music Therapy Today* (online journal of music therapy) (December 2007, latest issue published December 2007);
11. *Voices* (online international journal of music therapy) (March 2014);
12. *New Zealand Journal of Music Therapy* (March 2014);
13. *British Journal of Music Therapy* (March 2014);
14. Japanese Music Therapy Association Journal (March 2014);
15. Music and Medicine (March 2014).

We checked the bibliographies of relevant studies and reviews. We contacted relevant experts for the identification of unpublished trials.

We imposed no language restrictions for either searching or trial inclusion.

Data collection and analysis

Selection of studies

One author (JB) scanned the titles and abstracts of each record retrieved from the searches for the original review, while a research assistant did this for the update. If information in the abstract clearly indicated that the trial did not meet the inclusion criteria, we rejected the trial. When a title or abstract could not be rejected with certainty, the authors independently inspected the full-text article for the original review. This inspection was completed by JB and a research assistant for the update. We used an inclusion criteria form to assess the trial's eligibility for inclusion. We checked the inter-rater reliability for trial selection. If a trial was excluded, we kept a record of both the article and the reason for exclusion.

Data extraction and management

The lead author (JB) and a research assistant independently extracted data from the selected trials using a standardized coding form. There were no disagreements in the data extraction.

Assessment of risk of bias in included studies

JB and a research assistant assessed all included trials for risk of bias in the original review and were blinded to each other's assessments. For the updated review, JB and CD completed these assessments independently. Any disagreements were resolved by discussion. The authors used the following criteria for quality assessment.

Random sequence generation

- Low risk
- Unclear risk
- High risk

Random sequence generation was rated as low risk if every participant had an equal chance to be selected for either condition and if the investigator was unable to predict which treatment the participant would be assigned to. Use of date of birth, date of admission, or alternation resulted in high risk of bias.

Allocation concealment

- Low risk methods to conceal allocation included:
-
    - central randomization;
    - serially numbered, opaque, sealed envelopes;
    - other descriptions with convincing concealment.
- Unclear risk, authors did not adequately report on method of concealment.
- High risk (e.g., alternation methods were used).

Blinding of participants and personnel

- Low risk
- Unclear risk
- High risk

Since participants cannot be blinded in a music intervention trial, studies were not downgraded for not blinding the participants. As for personnel, in music therapy studies music therapists cannot be blinded because they are actively making music with the patients. In contrast, in music medicine studies blinding of personnel is possible by providing control group participants with headphones but no music (for example, a blank CD). Therefore, downgrading for not blinding personnel was only applied in studies that used listening to pre-recorded music.

Blinding of outcome assessors

- Low risk
- Unclear risk
- High risk

Incomplete outcome data

We recorded the proportion of participants whose outcomes were analysed. We coded losses to follow-up for each outcome as:

- low risk, if fewer than 20% of patients were lost to follow-up and reasons for loss to follow-up were similar in both treatment arms;
- unclear risk, if loss to follow-up was not reported;
- high risk, if more than 20% of patients were lost to follow-up or reasons for loss to follow-up differed between treatment arms.

Selective reporting

- Low risk, reports of the study were free of suggestion of selective outcome reporting
- Unclear risk
- High risk, reports of the study suggest selective outcome reporting

Other sources of bias

- Low risk
- Unclear risk
- High risk

Information on potential financial conflicts of interest was considered as a possible source of additional bias.
The above criteria were used to give each article an overall quality rating, based on the *Cochrane Handbook for Systematic Reviews of Interventions* Section 8.7 (Higgins 2011).
A. Low risk of bias: all criteria met.
B. Moderate risk of bias: one or more of the criteria only partly met.
C. High risk of bias: one or more criteria not met.
Studies were not excluded based on a low quality score.

Measures of treatment effect

All outcomes but one in this review were presented as continuous variables. We calculated standardized mean differences with 95% confidence intervals (CI) for outcome measures using results from different scales. When there were sufficient data available from various studies using the same measurement instrument, we computed a mean difference (MD) with 95% CI. For one outcome (that is mortality) we calculated the risk ratio with 95% CI.

Unit of analysis issues

In all studies included in this review, participants were individually randomized to the intervention or the standard care control group. Post-test values or change values on a single measurement for each outcome from each participant were collected and analysed.

Dealing with missing data

We analysed data on an endpoint basis, including only participants for whom a final data point measurement was obtained (available case analysis). We did not assume that participants who dropped out after randomization had a negative outcome.

Assessment of heterogeneity

We investigated heterogeneity using visual inspection of the forest plots as well as the I^2 statistic, with $I^2 > 50\%$ indicating significant heterogeneity.

Assessment of reporting biases

We tested for publication bias visually in the form of funnel plots (Higgins 2011).

Data synthesis

We entered all trials included in the systematic review into Review Manager (RevMan 5.2). We anticipated that some individual studies would have used final scores whereas others might have used change scores. We combined these different types of analyses as mean difference (MD). We calculated pooled estimates using the more conservative random-effects model. We determined the levels of heterogeneity by the I^2 statistic (Higgins 2002).
The following treatment comparison was made: music interventions versus standard care alone.

Subgroup analysis and investigation of heterogeneity

The following subgroup analyses were determined a priori, but these could not be carried out because of insufficient numbers of studies:

a. type of intervention (music therapy or music medicine);
b. dosage of music therapy or music medicine; and
c. music preference.

Subgroup analyses would have been conducted as described by Deeks et al (Deeks 2001) and as recommended in section 9.6 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Sensitivity analysis

The influence of study quality was examined using a sensitivity analysis wherein the results of including and excluding lower quality studies in the analysis were compared. Specifically, we assessed the impact of studies that used alternate group assignment as a randomization method.

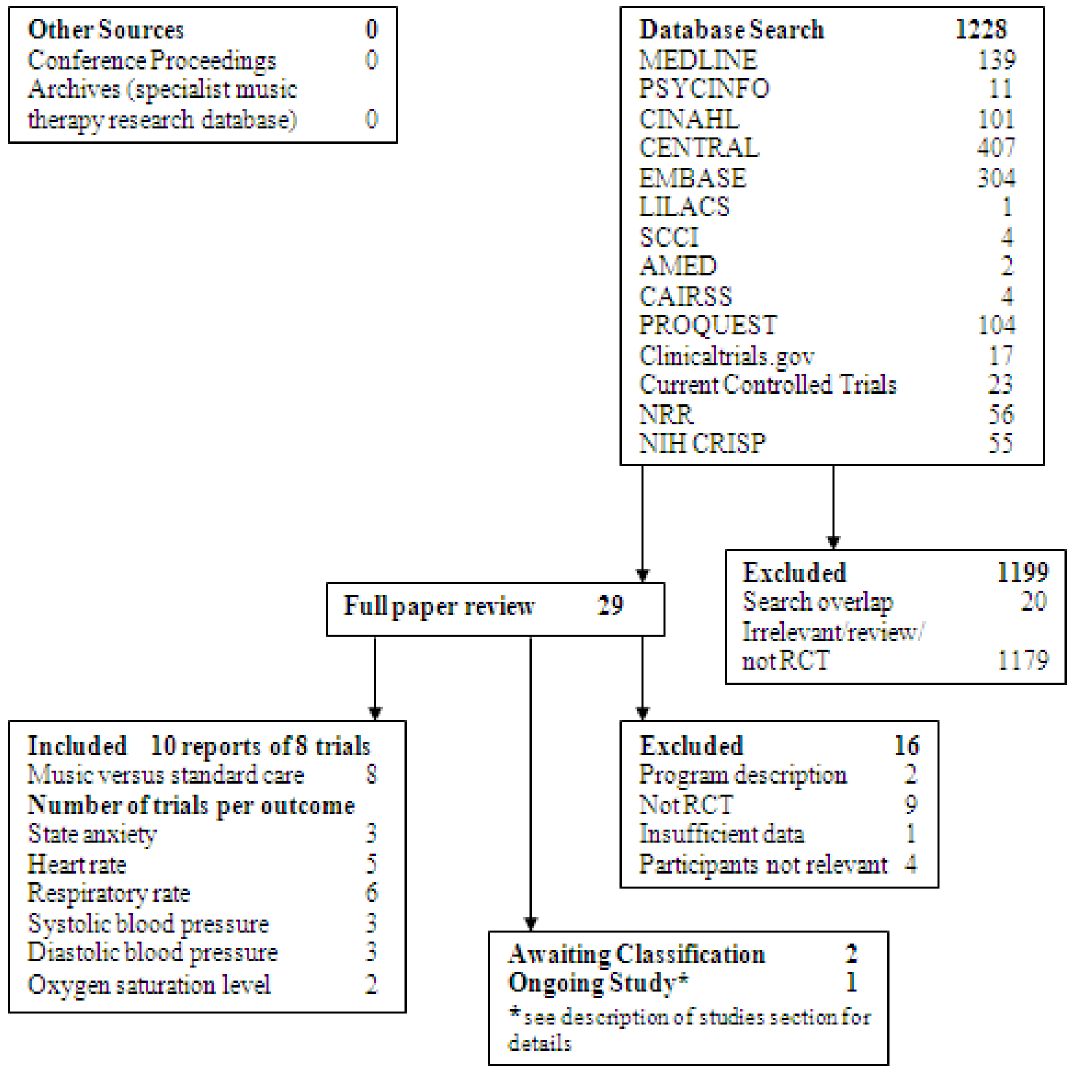
RESULTS

Description of studies

Results of the search

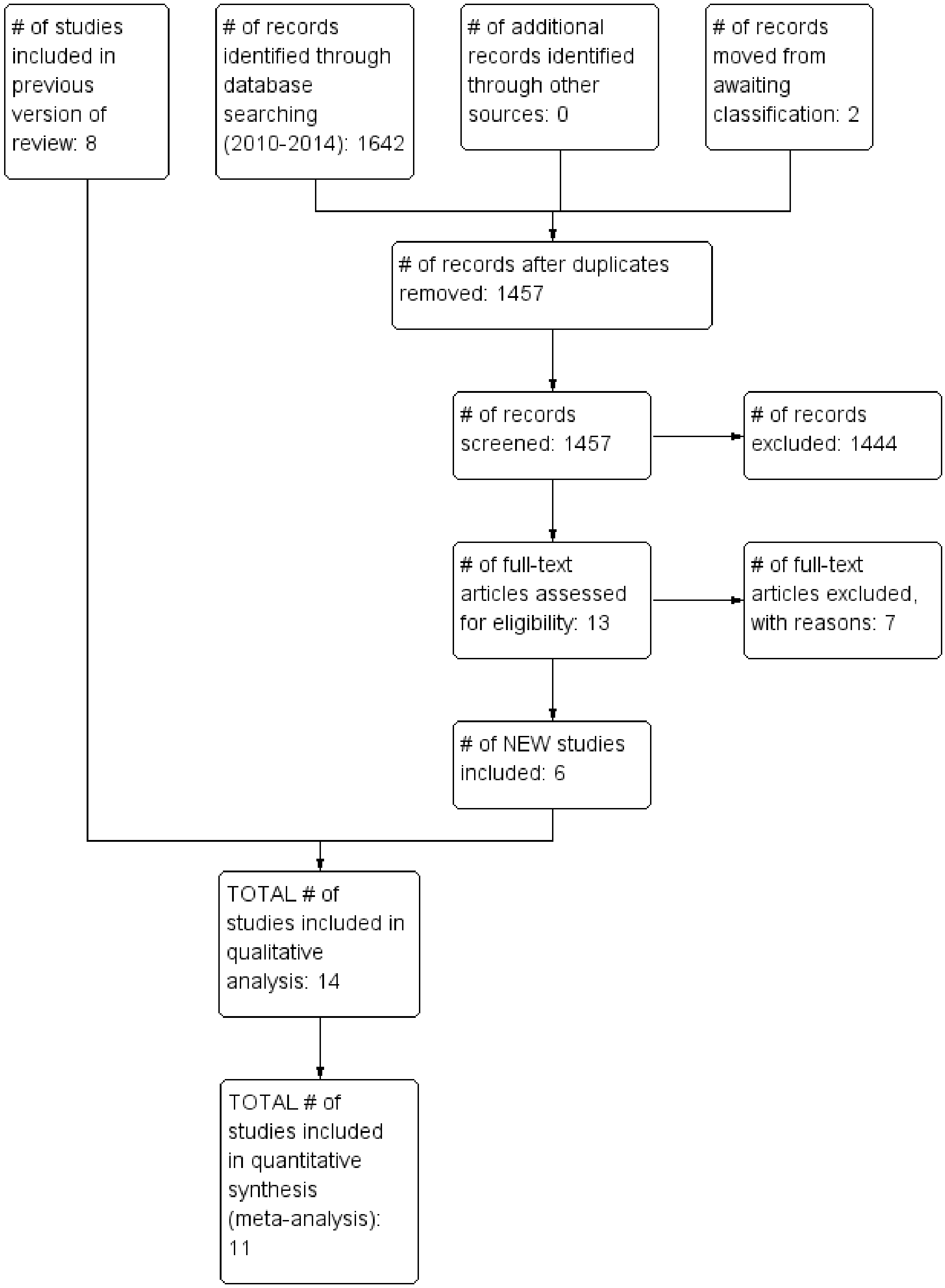
The database searches and handsearching of conference proceedings, journals, and reference lists resulted in 1228 citations (see Figure 1) for the original review. One author (JB) examined the titles and abstracts and identified 29 studies as potentially relevant, which were retrieved for further assessment. These were then independently screened by the two authors.

Figure 1. Study Flow Diagram - Original Review.



The 2014 update of the search resulted in 1557 extra citations (Figure 2). One review author (JB) and research assistant examined the titles and abstracts and retrieved full-text articles where necessary. This resulted in the addition of seven references reporting six new studies.

Figure 2. Study flow diagram - updated review.



Seventeen references reporting 14 trials were included in this review (see Characteristics of included studies) (Beaulieu-Boire 2013; Chlan 1995; Chlan 1997; Chlan 2007a; Chlan 2013; Conrad 2007; Dijkstra 2010; Han 2010; Jaber 2007; Korhan 2011; Lee 2005; Phillips 2007; Wong 2001; Wu 2008). Where necessary, we contacted chief investigators to obtain additional information on study details and data.

Included studies

We included 14 studies with a total of 805 patients in this review. These studies examined the effects of music on physiological and psychological outcomes in mechanically ventilated patients. Slightly more patients included in these studies were male (58%). The average age was 58 years. Eight studies provided details on ethnicity (Chlan 1997; Chlan 2007a; Chlan 2013; Han 2010; Korhan 2011; Lee 2005; Wong 2001; Wu 2008). For four of those studies (Chlan 1997; Chlan 2007a; Chlan 2013; Korhan 2011) the participants were predominantly white. For the other four studies all participants were Asian. Five studies were conducted in the USA (Chlan 1995; Chlan 1997; Chlan 2007a; Chlan 2013; Phillips 2007); three in China (Han 2010; Lee 2005; Wong 2001); one in Taiwan (Wu 2008); one in Canada (Beaulieu-Boire 2013); one in Germany (Conrad 2007); one in the Netherlands (Dijkstra 2010); one in Turkey (Korhan 2011); and one in France (Jaber 2007). Trial sample size ranged from 10 to 266 participants.
Eight studies (Beaulieu-Boire 2013; Chlan 1997; Chlan 2007a; Dijkstra 2010; Han 2010; Korhan 2011; Lee 2005; Wong 2001) included details on the ventilatory support modes used. Synchronized intermittent mandatory ventilation and the pressure support mode were most frequently used. Five studies (Han 2010; Jaber 2007; Lee 2005; Wong 2001; Wu 2008) detailed the type of airway management. The majority of the patients had an oral endotracheal tube or a tracheostomy tube. Few patients had a nasal endotracheal tube. Eleven studies (Beaulieu-Boire 2013; Chlan 1995; Chlan 1997; Chlan 2007a; Chlan 2013; Dijkstra 2010; Han 2010; Korhan 2011; Lee 2005; Wong 2001; Wu 2008) provided information related to the average number of days on mechanical ventilation before the onset of the study. The average number of days was 8.53 with a range of 0 days to 161 days. All patients were alert.
A variety of medical diagnoses were included in each study, except for Conrad (Conrad 2007), with the primary diagnoses being pulmonary-related problems in most studies. Other medical problems included post-surgical complications, cardiac disease, trauma injuries, cancer, and sepsis. Conrad's study only included postoperative patients. Not all studies measured all outcomes identified for this review.
Details of the studies included in the review are shown in the table Characteristics of included studies.

Thirteen studies were categorized as music medicine studies (as defined by the review authors in the background section). One study (Phillips 2007) was categorized as music therapy. All music medicine studies used music listening as the main intervention. The music therapy study used live music selected by the patient. The music therapist initially matched the music to the respiratory rate of the patient. The tempo of the music was then gradually decelerated to decrease the rate of vital signs to ranges suitable for extubation.
Most studies offered one 20 to 30-minute music session to the patients. Three studies offered 60-minute sessions (Beaulieu-Boire 2013; Chlan 2007a; Korhan 2011). Three studies offered two or more music sessions (Beaulieu-Boire 2013; Chlan 2013; Dijkstra 2010). In most clinical settings that serve patients on mechanical ventilation, listening to pre-recorded music can be easily implemented at low cost. However, studies are needed that compare the effect of different frequencies, durations, and timing of music sessions. Offering multiple music listening sessions allows for the patient to give feedback about the music, select different music if needed, and become more skilled in using music for relaxation purposes. In the case of music therapy interventions, multiple sessions allow for the development of a therapeutic relationship and deepening of the therapeutic process through the music. This may lead to greater health benefits.
Except for one study (Conrad 2007), none of the music medicine studies in the original review provided detailed information about the music that was used. The authors only reported the different styles of music that were offered to the participants (for example, jazz, easy listening, country and western, classical music) without any composition-specific or performance-specific information. Conrad provided information about the specific compositions that were used (see Characteristics of included studies table). Only one study (Chlan 1997) provided tempo information. Four of the six studies that were included in the update reported more details regarding the music that was used (Beaulieu-Boire 2013; Dijkstra 2010; Han 2010; Korhan 2011). One study (Chlan 2013) conducted a detailed assessment of music preference with each patient and personalized playlists were used.
Eleven studies used patient-selected music, whereas three studies (Beaulieu-Boire 2013; Conrad 2007; Korhan 2011) used researcher-selected music. In some trials, only classical music choices were offered without a good rationale for this music selection. In several trials, participants were allowed to select the music from a variety of music that was offered. This decision was based on the assumption that music preference plays an important part in the effectiveness of music relaxation. However, it needs to be noted that participants could only select from a limited number of music styles presented by the researcher. It is likely that the preferred music of some of the participants was not included in the music selec-

tion offered and, even if it were, that they may not have liked the specific compositions or songs being played. Lee explicitly stated that four participants disliked the music (Lee 2005). Another researcher reported that five patients refused to participate because they disliked the music selections that were being offered, whereas five other participants expressed a dislike for the music after they completed participation in the music intervention (Wong 2001). An exception to this were the trials by Chlan 2013 and Han 2010. In the study by Chlan and colleagues, a music therapist conducted detailed assessments of patient preferences. Han offered participants over 40 pieces of music in a variety of styles to select from.

The data for one study (Chlan 2007a) could not be pooled with the other studies because of severe validity issues. The lead author expressed the following concerns: there was wide variability in mean levels of biomarkers, a very small sample size, and several confounding factors (for example, administration of intravenous morphine sulphate to two control patients; and two experimental patients needed endotracheal suctioning during the intervention). The data for two additional studies (Conrad 2007; Korhan 2011) were only provided in narrative form in this review because of insufficient data reporting. Finally, the data from the study by Chlan and colleagues (Chlan 2013) could not be pooled with other studies because the report detailed the results of statistical modelling but did not provide means and SDs.

Excluded studies

In the original review, we excluded a total of 16 studies for the following reasons: (a) programme descriptions only (Chlan 2000; Fontaine 1994); (b) studies were not randomized controlled trials or controlled clinical trials (Besel 2006; Burke 1995; Chlan 2001; Chlan 2006; Chou 2003; Hansen-Flachen 1994; Hunter 2010; Iriarte 2003; Twiss 2006); (c) study participants did not meet the inclusion criteria (Caine 1991; Lorch 1994; Standley 1995; Wiens 1995); and (d) insufficient data reporting (Almerud 2003).

For the update, we excluded an additional seven studies for the following reasons: (a) studies were not randomized controlled trials or controlled clinical trials (Chlan 2011); (b) no music intervention (Tate 2010); (c) review article (Austin 2010; Davis 2012; Ho 2012); and (d) a commentary (Bauer 2002; Nilsson 2011).

The reasons for exclusion are listed in the table Characteristics of excluded studies.

Risk of bias in included studies

Allocation

We included studies that used appropriate methods of randomization (for example, a computer-generated table of random numbers, drawing of lots, flip of coins) (11 studies) (Beaulieu-Boire 2013; Chlan 1995; Chlan 1997; Chlan 2007a; Chlan 2013; Dijkstra 2010; Han 2010; Jaber 2007; Lee 2005; Wong 2001; Wu 2008) as well as studies that used non-random methods of allocation (for example, alternate group assignment) (three studies) (Conrad 2007; Korhan 2011; Phillips 2007). The impact of method of randomization was examined by sensitivity analyses. Fifty-seven per cent of the studies (eight studies) used allocation concealment (Beaulieu-Boire 2013; Chlan 1995; Chlan 1997; Chlan 2007a; Chlan 2013; Lee 2005; Wong 2001; Wu 2008) and for three studies (21%) the use of allocation concealment was unclear (Han 2010; Jaber 2007; Korhan 2011).

Blinding

In music intervention studies, participants cannot be blinded (unless they are in studies that compare different types of music interventions). Three studies reported blinding personnel (Beaulieu-Boire 2013; Conrad 2007; Lee 2005). This was achieved by having both music group and control group participants wear headsets and listen to a CD. The control group listened to a blank CD.

Only five trials reported blinding of the outcome assessors for objective outcomes (Beaulieu-Boire 2013; Conrad 2007; Dijkstra 2010; Jaber 2007; Lee 2005). For two trials the use of blinding was unclear (Chlan 2013; Phillips 2007). The other trials did not use blinding for objective outcomes. For subjective outcomes, (for example, the State and Trait Anxiety Inventory (STAI) (Spielberger 1983)), blinding of outcome assessors was not possible unless the participants were blinded to the intervention. We would like to point out that the assessment of risk of bias figure lists several studies as having used blinding for subjective outcomes. However, these were studies that did not include subjective outcomes. A rating of low risk was assigned if studies did not include subjective outcomes.

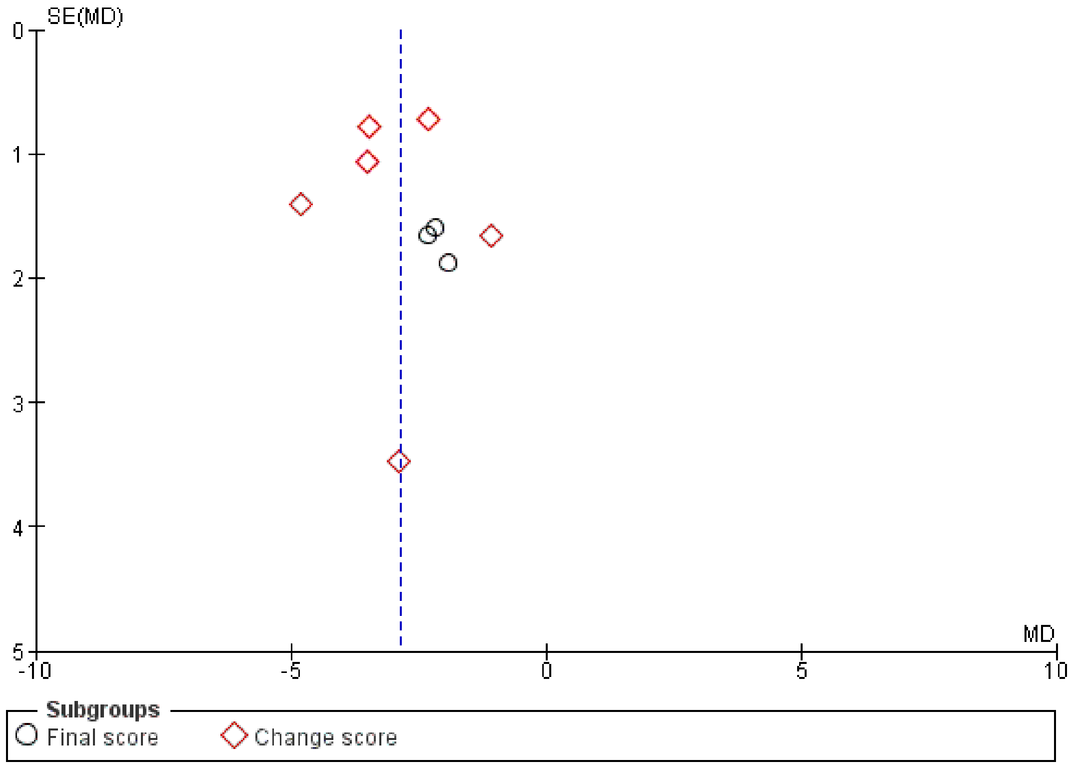
Incomplete outcome data

The dropout rate was small for most trials, namely between 0% and 11%. One trial (Chlan 2013) reported a dropout rate of more than 20%. For three trials it was unclear whether there were any participant withdrawals (Korhan 2011; Lee 2005; Wong 2001) . Most trials reported reasons for dropout. Detailed information on the dropout rates and reasons is included in the Characteristics of included studies table.

Selective reporting

Publication bias for respiratory rate as an outcome was examined visually in the form of a funnel plot (Figure 3). The funnel plot suggests that all but one of the included studies had small standard errors (that is they were plotted towards the top of the graph). Publication bias may be present in that no studies were included with findings that were not statistically significant.

Figure 3. Funnel plot of comparison: 1 Music versus standard care, outcome: 1.4 Respiratory rate.



Other potential sources of bias

We did not identify any other potential sources of bias in the studies included in this review.

As a result of the risk of bias assessment, we concluded that one trial was at low risk of bias (Beaulieu-Boire 2013). All other trials were at high risk of bias. The main reason for receiving a high risk of bias rating was the lack of blinding. As mentioned before, blinding is often impossible in music therapy and music medicine studies that use subjective outcomes, unless the music intervention is compared to another treatment intervention (for example, progressive muscle relaxation or a different type of music intervention). Therefore, it appears impossible for these types of studies to receive a low or moderate risk of bias even if all other risk factors (for example, randomization, allocation concealment, etc.) have been adequately addressed.

As all but one trial were rated at the same level (high risk), we did not carry out sensitivity analysis on the basis of overall quality rating. Instead, we conducted a sensitivity analysis to examine the impact of the method of random sequence generation. Excluding those studies that used alternate assignment or for which the randomization method was unclear did not alter the findings of this review. Specific sensitivity analysis findings are reported in the Effects of interventions section.

Risk of bias is detailed for each trial in the risk of bias tables included in the Characteristics of included studies table, and the 'Risk of bias' summary (Figure 4). In addition, an overall assessment of risk of bias can be viewed in Figure 5.

Figure 4. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

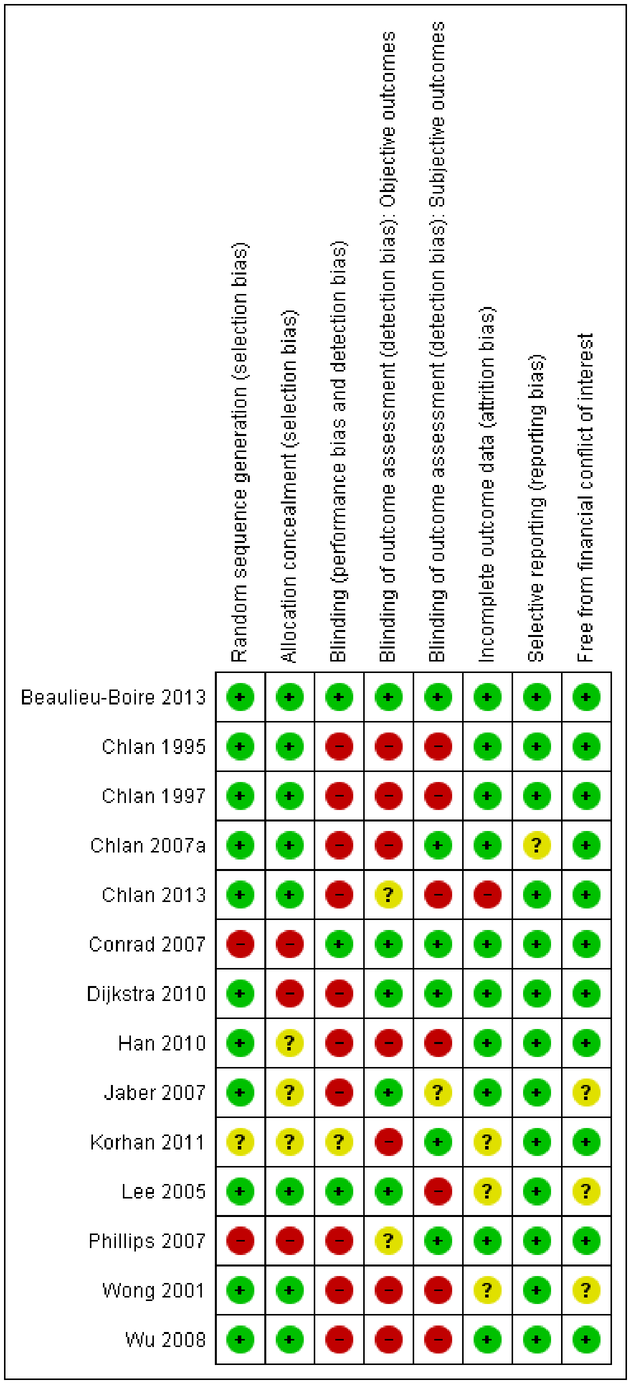
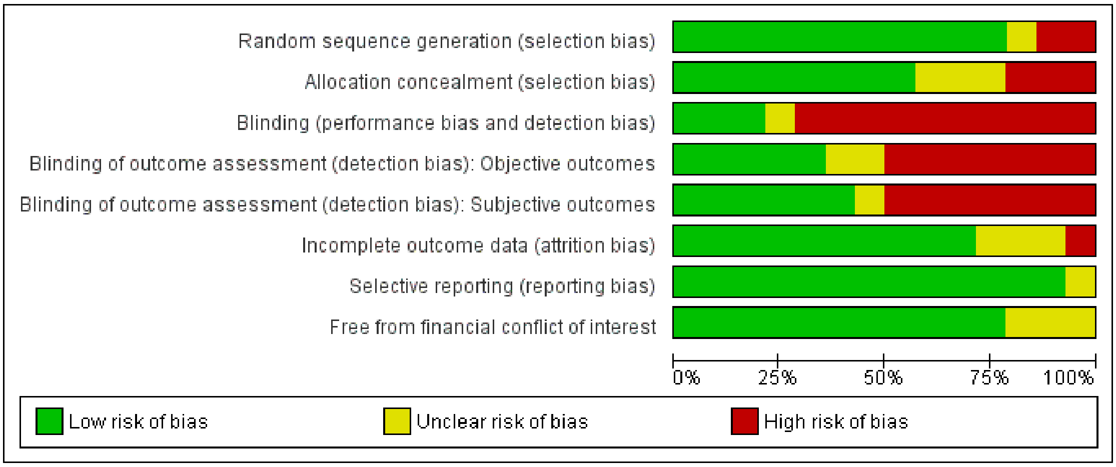


Figure 5. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Effects of interventions

See: **Summary of findings for the main comparison** Music compared to standard care for mechanically ventilated patients

Primary outcomes

State anxiety

Six studies (Chlan 1997; Chlan 2013; Han 2010; Lee 2005; Wong 2001; Wu 2008) examined the effects of music listening on state anxiety in mechanically ventilated patients. Four studies (Chlan 1997; Han 2010; Lee 2005; Wong 2001) used the Spielberger State and Trait Anxiety Inventory (STAI), State Anxiety Short Form, whereas the other studies used a visual analogue scale for anxiety (VAS-A) (Chlan 2013; Wu 2008). The pooled estimate of five of these studies (N = 288) indicated that music listening may have a beneficial effect on anxiety (SMD -1.11, 95% CI -1.75 to -0.47, P = 0.0006). Statistical heterogeneity across the trials (I^2 = 83%) was due to some trials (Chlan 1997; Han 2010) reporting much larger beneficial effects of music interventions than others (Analysis 1.1).

The study by Chlan and colleagues (Chlan 2013) was not included in any of the meta-analyses because the authors presented their findings as statistical modelling results and not as post-test means or change scores with respective standard deviations (SDs). Therefore, the findings of this study were only reported in the narrative. Chlan (Chlan 2013) reported the results of statistical modelling that used either sedation frequency or sedation intensity. The models suggested that music listening lowered VAS-A scores consistently by more than 19 mm on the VAS (sedation frequency ß -19.5, 95% CI -32.2 to -6.8; sedation intensity ß -19.3, 95% CI -32 to -6.6; P = 0.003 for both) compared to usual care.

Secondary outcomes

Sedative and analgesic drug intake

Three studies (Beaulieu-Boire 2013; Chlan 2013; Conrad 2007) provided data on the effect of music on sedative and analgesic drug intake. Beaulieu-Boire reported separate data for intake of fentanyl, benzodiazepines, and propofol. Chlan reported data on sedation intensity and sedation frequency. Sedation intensity was computed by "dose amounts of medications from disparate drug classes by using a weight-adjusted dose (adjusting for differing patient weights) of each sedative administered during 4-hour time blocks during mechanical ventilation" (p. 2336) (for additional information on these computations see Chlan 2013). Sedation frequency score was computed by dividing "a 24-hour day into six 4-hour time blocks and, for each of the 8 drugs, the occurrences in which a sedative was administered at least once during that interval were summed. This approach to sedative exposure accounts for medications administered to patients from nonequivalent, disparate drug classes" (p. 2337). Conrad only provided a narrative summary of the findings on propofol consumption.

Beaulieu-Boire and colleagues (Beaulieu-Boire 2013) reported a trend toward reduction in fentanyl daily consumption for the music listening group (means ± SD: 1597 ± 1418 μg pre- and 1343 ± 1342 μg post-music versus 1593 ± 1986 μg pre- and 1715 ± 1859 μg post-control) but the difference between the two groups was not statistically significant (P = 0.06). There was no difference between the groups for the intake of other sedative drugs. For daily consumption of benzodiazepines, the following means and SDs were reported: 42 ± 88 mg pre- and 36 ± 94 mg post-music versus 46 ± 107 mg pre- and 45 ± 109 mg post-control). For propofol daily consumption, the following means and SDs were reported: 291 ± 732 mg pre- and 284 ± 730 mg post-music versus 282 ± 677 mg pre- and 395 ± 928 mg post-control.

Chlan (Chlan 2013) reported that the music listening group had a greater decrease in change over time of the sedation intensity score (ß -0.18, 95% CI -0.36 to -0.004, P = 0.05) as well as the sedation frequency score (ß -0.21, 95% CI -0.37 to -0.05, P = 0.01) compared with the usual care group. The authors also reported group differences for the fifth study day, which represented the average time patients were enrolled in the study. Whereas an average usual care group participant received five doses of any one of the eight commonly administered sedative and analgesic medications (midazolam, lorazepam, propofol, dexmedetomidine, morphine, fentanyl, hydromorphone, and haloperidol), an equivalent music group participant received just three doses. In terms of sedation intensity scores, an average usual care participant had a sedation intensity score of 4.4 whereas an equivalent music listening group participant had a sedation intensity score of 2.8. This represented a relative reduction of 38% for sedation frequency score and 36% for sedation intensity score.

Conrad (Conrad 2007) reported that "patients in the music group did not require additional sedation by propofol, whereas among patients in the control group, propofol was occasionally necessary to allow sufficient patient-ventilator coordination" (p. 2710). Other authors reported that, as part of the protocol, no medication was provided to the participants for the duration of the intervention (Chlan 1995; Jaber 2007).

One study (Dijkstra 2010) examined the effect of music listening on level of sedation by means of Ramsay scores rather than on sedative drug intake. Significantly higher sedation scores were obtained in the music listening group compared to the control group after the first session (MD 6.60, 95% CI 5.64 to 7.56, P < 0.0001). A trend for higher scores in the music group remained for the second and third sessions but these were no longer statistically significant.

Heart rate

The pooled estimate of eight studies (Chlan 1995; Chlan 1997; Dijkstra 2010; Han 2010; Jaber 2007; Lee 2005; Phillips 2007; Wu 2008) (N = 338) indicated that listening to music significantly reduced heart rate (MD -3.95, 95% CI -6.62 to -1.27, P = 0.004; I^2 = 62%). The results were not consistent across studies with seven studies reporting a greater heart rate reduction in the music listening group compared to the control and one study (Wu 2008) reporting a slightly greater reduction in the control group (Analysis 1.2). A sensitivity analysis examining the impact of randomization methods revealed that inclusion of an alternate assignment study (Phillips 2007) did not inflate the effect size. In contrast, excluding this study led to a higher pooled estimate (MD -4.01, 95% CI -6.80 to -1.22, P < 0.005) (Analysis 1.3).

Conrad (Conrad 2007) reported that the heart rate in the control group increased from 120 beats per minute (BPM) (SD = 9) to 125 bpm (SD = 7), whereas it remained the same in the music group. However, no significant differences between the groups were found. Because no means and SDs were reported for the music group, these data could not be included in the meta-analysis. Conrad was unable to provide the original data.

One cross-over study (Beaulieu-Boire 2013) reported that music listening did not alter overall vital signs (heart rate, respiratory rate, and arterial blood pressure) compared with the placebo-control condition but no statistical information was provided. The authors were unable to provide means and SDs for these outcomes.

Respiratory rate

Listening to music also had a significant effect on respiratory rate (9 studies, N = 357; MD -2.87, 95% CI -3.64 to -2.10, P < 0.00001) and the results were consistent across studies (I^2 = 0%) (Analysis 1.4) (Chlan 1995; Chlan 1997; Dijkstra 2010; Han 2010; Jaber 2007; Lee 2005; Phillips 2007; Wong 2001; Wu 2008). One study (Korhan 2011) could not be included in the meta-analysis because no means and SDs were reported. The results of this study indicated a statistically significant difference between the music group and the control group for respiratory rate (P = 0.04).

A sensitivity analysis excluding the Phillips study (Phillips 2007) because of its inadequate randomization method did not change the pooled estimate (MD -2.87, 95% CI -3.64 to -2.09, P < 0.00001; I^2 = 0%) (Analysis 1.5).

Blood pressure

Seven studies (Chlan 1995; Dijkstra 2010; Han 2010; Jaber 2007; Korhan 2011; Lee 2005; Wu 2008) examined the effects of music listening on blood pressure. The study by Korhan (N = 60) could not be included in the meta-analysis because of lack of statistical information. The pooled estimate of the other studies (N = 269) indicated a beneficial effect for the music intervention on systolic blood pressure (SBP) (MD -4.22, 95% CI -6.38 to -2.06, P = 0.0001) that was consistent across studies (I^2 = 0%) (Analysis 1.6). A pooled estimate of -2.16 mm Hg (95% CI -4.40 to 0.07) was found for diastolic blood pressure (DBP), however this effect was not statistically significant (P = 0.06). (Analysis 1.7). Korhan reported a statistically significant difference between the music group and the control group for SBP (P = 0.02) and DBP (P = 0.02).

The pooled estimate of three studies (Dijkstra 2010; Wong 2001; Wu 2008) indicated no strong evidence of effect for the music intervention on mean arterial pressure (MAP) (MD -1.79, 95% CI -4.56 to 0.99, P = 0.21; I^2 = 0%) (Analysis 1.8). In contrast, Conrad (Conrad 2007) reported a significant difference (P = 0.014) between the intervention group (N = 5) and the control group (N = 5) but no means and SDs were provided and, therefore, these study results could not be pooled with the results of the other studies.

Oxygen saturation levels

Five studies examined the effects of music listening on oxygen saturation levels (Chlan 1995; Han 2010; Korhan 2011; Phillips 2007; Wu 2008). The study by Korhan could not be included in the meta-analysis because of lack of statistical information. In the pooled estimate the four remaining studies did not find support for an effect of music (MD -0.05, 95% CI -0.67 to 0.57, P = 0.88; I^2 = 42%) (Analysis 1.9). Similarly, Korhan (Korhan 2011) did not find a statistically significant difference between the music group and the control group for this outcome (P = 0.86). Chlan (Chlan 1995) commented that the lack of improvement in oxygen saturation level may be due to the fact that when a patient was already 100% saturated, there could be no increase in oxygen saturation level. She suggested that mixed venous oxygen saturation monitoring may be a more sensitive measure for oxygen consumption.

Hormone levels

Conrad (Conrad 2007) obtained blood samples for the participants before and after the intervention to measure concentrations of dehydroepiandrosterone (DHEAS), growth hormone, epinephrine, norepinephrine, adrenocorticotrophic hormone (ACTH), cortisol, interleukin-6 (IL-6), prolactin, and prolactin monomer. Conrad examined the effects of music listening on these hormone levels in an attempt to elucidate the physiological mechanisms by which music may have a stress-reducing effect. The specific neuroendocrine outcomes were selected based on current literature on the human neurohormonal stress response (Conrad 2007). Significant differences were found between the music and the control groups for DHEAS (P = 0.011), growth hormone (P = 0.032), IL-6 (P = 0.028), and epinephrine (P = 0.014). No significant between-group differences were found for prolactin (P = 0.27), prolactin monomer (P = 0.08), norepinephrine (P = 0.22), ACTH (P = 0.36), or cortisol (P = 0.92). The sample size in this study was very small (N = 10) and no means and SDs were reported.

Likewise, Beaulieu-Boire and colleagues (Beaulieu-Boire 2013) examined the impact of music listening on hormone levels. Study outcomes included cortisol, ACTH/cortisol ratios, prolactin, IL-6, C-reactive protein (CRP), and methionine-enkephalin content (MET-enkephalin). The results indicated that cortisol levels decreased in the music listening group (mean ± SD: 815 ± 126 at pre-test, 727 ± 98 nmol/L at post-test) but not in the control group (741 ± 71 at pre-test, 746 ± 68 nmol/L at post-test) and this difference between the groups was statistically significant (P < 0.05). ACTH/cortisol ratios increased in the music listening group (+0.04 ± 0.016) but not in the control group (-0.028 ± 0.02) (P = 0.015). Music listening decreased blood prolactin levels (29.3 ± 3.5 μg/L at pre-test, 27.4 ± 3.4 μg/L at post-test) while no changes were found in the control group (28.8 ± 4.1 μg/L at pre-test, 28.4 ± 4 μg/L at post-test) (P < 0.05). Blood leptin and MET-enkephalin were not affected by music listening (leptin: 19 ± 4 ng/mL at pre-test, 19.6 ± 4 ng/mL at post-test; MET-enkephalin: 251 ± 63 pg/mL at pre-test, 252 ± 68 pg/mL at post-test). Finally, CRP levels did not change in the music condition or the control condition whereas IL-6 decreased in the music condition but this was not statistically significant (158 ± 29 pg/mL at pre-test, 147 ± 29 pg/mL at post-test, P = 0.11).

Chlan (Chlan 2007a) also obtained serum levels of stress hormones, including epinephrine, norepinephrine, corticotropin, and cortisol, but found no significant differences between the music group (N = 5) and the control group (N = 5). Chlan suspected that the results were influenced by the fact that two participants in the music group needed endotracheal suctioning before the blood sample was obtained. In addition, five participants in the rest control group received intravenous morphine sulfate immediately prior to or during the implementation of the protocol, potentially influencing the epinephrine and norepinephrine levels.

In a later study, Chlan and colleagues (Chlan 2013) examined the effects of patient-directed music (PDM) listening on urine free cortisol (UFC) levels in 65 mechanically ventilated participants. PDM did not result in greater reductions in UFC compared to the control group. The authors reported that the lack of statistical significance was likely due to the small sample size and the large variability among participants in UFC levels. Patterns of UFC in the music group did suggest a potential buffering effect as evidenced by less extreme values over time as compared to the increased UFC levels in the control group.

Mortality

Two studies reported data on mortality rates (Dijkstra 2010; Han 2010) during the hospital stay. Results suggested that music interventions did not have a statistically significant effect on mortality (RR 0.76, 95% CI 0.38 to 1.51, P = 0.43) (Analysis 1.10).

No studies were identified that addressed the other secondary outcomes listed in the protocol, namely quality of life, patient satisfaction, post-discharge patient outcomes, and cost-effectiveness.

DISCUSSION

Summary of main results

State anxiety

The results of six studies suggest that music listening may have a beneficial effect on anxiety in mechanically ventilated patients. Although the magnitude of the effect differed across the studies, the trials agreed on the direction of the point estimates. This anxiety-reducing result (SMD -1.11) is considered large in size according to interpretation guidelines put forth by Cohen (Cohen 1988). Cohen suggested that an effect size of 0.2 be considered a small effect, an effect size of 0.5 medium, and an effect size of 0.8 large.

Sedative and analgesic drug intake

One large-scale study reported a decrease in intake of sedatives and analgesics and one study reported a trend toward reduction in daily fentanyl consumption. A third study examined sedation levels of participants and found that music listening resulted in significantly higher levels of sedation after one session.

Physiological outcomes

The results of this review indicate that listening to music reduces heart rate but the results were not consistent across studies. Music listening reduces respiratory rate consistently across studies. A reduction in these physiological responses is considered indicative of a relaxation response.

Mixed results were found for blood pressure. According to six studies, music listening consistently reduces systolic blood pressure. However, those same studies found no strong evidence for the effect of music on diastolic blood pressure. Based on the results of three studies, no strong evidence was found for an effect of music listening on mean arterial pressure. These results indicate that the physiology underlying haemodynamic responses in mechanically ventilated patients is complicated and may be confounded by ventilator settings as well as medications.

Music listening did not improve oxygen saturation levels according to five studies. However, one could question the usefulness of oxygen saturation as an indicator of a relaxation response in mechanically ventilated patients as this outcome is greatly influenced by ventilator settings.

Mixed results were found for blood hormone levels with one study reporting greater improvements in the music listening group for DHEAS, growth hormone, IL-6, and epinephrine but not for prolactin, norepinephrine, ACTH, or cortisol. The lack of effect of music listening on cortisol (urinary free cortisol) was supported by another small study. However, a third study with a much larger sample size reported beneficial effects for music listening on cortisol, ACTH/cortisol ratios, and prolactin but not on leptin, MET-enkephalin, or IL-6.

Finally, two studies reported on mortality rates. No strong evidence was found for an effect of music listening.

No studies could be found that examined the effects of music interventions on quality of life, patient satisfaction, post-discharge outcomes, and cost-effectiveness in mechanically ventilated patients.

Overall completeness and applicability of evidence

Results of this review indicate that music listening consistently reduces anxiety in mechanically ventilated patients and this difference is considered large and clinically significant. This relaxation response is supported, in part, by results of the effects of music listening on physiological responses. In addition, some trials suggested a beneficial effect of music listening on sedative and analgesic drugs intake but more research is needed in this area before this evidence can influence clinical decision-making.

All but one trial (Phillips 2007) used listening to pre-recorded music as the clinical intervention and were categorized as music medicine intervention trials. This prevented us from addressing the third objective of this review, namely to compare the effects of different types of music interventions. It remains unclear whether music therapy interventions, using live music to meet specific in-the-moment needs of the patients, are more effective than listening to pre-recorded music. Furthermore, most trials used patient-selected music. Therefore, we could not address the second objective of this review, namely to compare the use of patient-selected versus researcher-selected music.

All but three trials (Beaulieu-Boire 2013; Chlan 2013; Dijkstra 2010) used one music intervention session. In the original review we posed questions about the relationship between the frequency and duration of treatment and treatment effect, and recommended further investigation into the optimal frequency and duration of music interventions for critically ill patients. Chlan and colleagues (Chlan 2013) conducted a study examining this very question. In their study, patients were asked to self-direct the use of music for anxiety management; they could listen to music whenever they wanted and for as long as they desired. Participants used headphones that contained a data logger system to capture each PDM session and the total daily music listening time. Participants listened to music for an average 79.8 (SD = 126) minutes per day. The authors presented statistical modelling results that suggested that sedation frequency decreased by an average of 0.17 points per day for all patients, regardless of group assignment. However, for patients in the music listening group the dose frequency decreased by another 0.21 points per day. Frequency dose was furthermore influenced by age and gender. The authors explained that their patient-directed music (PDM) protocol was modelled on the patient-controlled analgesia (PCA) intervention, an intervention that has been shown to result in better pain control and patient satisfaction (Chlan 2013). The authors continued that the PDM protocol "empowers patients in their own anxiety management" (p. 2340). The results of this study suggested that patients, on average, opt to listen to music more or longer, or both, than what has been implemented in other research studies (namely one 30-minute session).

Presently, no data can be provided regarding costs or cost-effectiveness of music medicine applications in the care of mechanically ventilated patients as these data were not included in the studies reviewed. Furthermore, no data were provided regarding costs for music therapy interventions; therefore, no comparisons can be conducted between these two types of treatments. It is recommended that future research include cost-effectiveness measures of these two interventions as well as cost comparisons between them.

Trials included in the original review, in general, included very limited information about the music selections used, except for mentioning general music styles (for example, classical, easy listening, jazz, country). Several trials included in the update of this review reported greater details about the music selections that were used. Because music within each music style can vary widely, it is important that researchers continue to provide detailed information regarding music selections as this is useful for clinical decision-making. Details on specific music selections for each study can be found in the Characteristics of included studies table.

None of the studies included children. Therefore, these results cannot be generalized to a paediatric population.

Because little information was provided in these studies about the ethnic make-up of the patient samples, one can question the generalizability of these results to various ethnic groups. Persons' cultures may influence their music preferences and their potential acceptance and use of music as a therapeutic agent, especially during high-stress medical situations such as mechanical ventilation. This in turn may influence the anxiety-reducing potential of music, in greater or lesser degrees.

Quality of the evidence

In general the quality of reporting was poor, with only four studies detailing the methods of randomization and allocation concealment, and level of blinding (Beaulieu-Boire 2013; Lee 2005; Wong 2001; Wu 2008). The chief investigators of most studies needed to be contacted to provide additional methodological and statistical information. All but one study (Beaulieu-Boire 2013) received a high risk of bias rating.

Because of the large number of trials at high risk of bias, the findings of this review need to be interpreted with caution. It is important to be mindful that many studies received a high risk of bias rating because of lack of blinding. Often blinding of participants is not possible in music medicine or music therapy studies unless a comparative design is used (for example, comparing listening to pre-recorded music with interactive music making with a therapist). When participants cannot be blinded to the intervention, there is definitely an opportunity for bias when participants are asked to report on subjective outcomes such as anxiety. However, this also means that trials that meet all other requirements for a low risk of bias rating are assigned a high risk of bias because of the inability to meet the blinding requirement for subjective outcomes.

For anxiety, respiratory rate, and systolic blood pressure, consistent effects were obtained across studies. For the other outcomes included in the protocol inconsistent results were obtained or not enough studies were available. Most trials that were included were small (average n = 57; range of sample size 10 to 266), except for Chlan 2013 (n = 266) and Han 2010 (n = 137). This resulted in a lack of precision of treatment effects as evidenced by the rather large confidence intervals. This, combined with the high risk of bias, requires that the results of this review be interpreted with caution.

In summary, the quality of evidence was low (Summary of findings for the main comparison).

Potential biases in the review process

This review included 14 trials. The strength of our review is that we searched all available databases and a large number of music therapy journals (in English, German, and French language), checked reference lists of all relevant trials, contacted relevant experts for identification of unpublished trials, and included publications without restricting language. In spite of such a comprehensive search, it is still possible we missed some published and unpublished trials. We requested additional data, where necessary, for all trials we considered for inclusion. This allowed us to get accurate information on the trial quality and data for most trials, and helped us make well-informed trial selection decisions.

It is possible that we did not identify some grey literature; however, it is doubtful that this would have had a significant impact on our results. Grey literature tends to include trials with relatively small numbers of participants and inconclusive results (McAuley 2000).

Agreements and disagreements with other studies or reviews

A review by Davis and Jones (Davis 2012) detailed study characteristics and statistical findings of seven individual clinical trials (English language only) on the use of music interventions with mechanically ventilated patients. The review authors did not provide a reason for not applying meta-analytic procedures to the study results. They concluded that "music therapy in ventilated patients is a safe and effective treatment" (p. 165). They recommended that future studies should investigate the impact of different music styles, and duration, and frequency of music listening. They furthermore recommended that future randomized controlled trials measure outcomes related to number of ventilator days, ICU stay, and hospital length of stay.

One review article (Austin 2010) on the use of music with paediatric patients on mechanical ventilation reported that no clinical trials with this population could be identified. The author did report on a music therapy case study with two children on mechanical ventilation and one clinical trial with cardiac paediatric patients in the ICU. Austin concluded that the lack of evidence on the use of music with mechanically ventilated paediatric patients, and the inability to generalize the results of clinical trials from adult to paediatric populations, prevented reaching conclusions about the effectiveness of music interventions with mechanically ventilated paediatric patients.

The aim of this review was to update the previous version (Bradt 2010) with the results of trials completed during the three years since its publication. Overall, the results of this review are similar to those of the previous version. The findings on state anxiety were strengthened because of additional studies. In addition, whereas there was no strong evidence for an effect on blood pressure in the previous review, the results of the updated review indicate a beneficial effect of music listening on systolic blood pressure. The review was expanded with some additional outcomes, namely sedative and analgesic intake, mean arterial pressure, and mortality. However, at this time, there were not enough studies to provide strong evidence for an effect of music interventions on these outcomes.

The anxiety-reducing effects of music interventions found in this review are consistent with the findings of three other Cochrane systematic reviews on the use of music with coronary heart disease patients (Bradt 2013b), cancer patients (Bradt 2011), and presurgical patients (Bradt 2013a).

AUTHORS' CONCLUSIONS

Implications for practice

This systematic review indicates that music listening may have beneficial effects on state anxiety in mechanically ventilated patients in critical care units. These results are consistent with the findings of three other Cochrane systematic reviews on the use of music for anxiety reduction, with coronary heart disease patients (Bradt 2013b), cancer patients (Bradt 2011), and surgical patients (Bradt 2013a). The findings of this meta-analysis further indicate that music listening may reduce physiological responses including the respiratory rate and systolic blood pressure. Because of these results, and because music listening is an easy intervention to implement, it is recommended that music listening be offered as a stress management intervention to these critically ill patients.

All studies in this review used sedative music or music that is calming. However, there are many styles of sedative music (for example, new age, classical, country and western, easy listening, etc.) and at this time it is unclear which type of music is most effective. The music therapy literature recommends that patients select music that is characterized by a slow tempo and lacks abrupt changes and sharp timbres. In addition, music that evokes strong emotional reactions, which may be caused by memories associated with the music, should be avoided when used for stress and anxiety reduction purposes (Dileo 2007). These recommendations stem from the clinical experience and knowledge of music therapists as well as experimental research in the field of music psychology. Chlan (Chlan 2000) emphasizes that effective application of music listening protocols with mechanically ventilated patients requires careful scrutiny of music selection according to patient preferences as well as musical elements that are considered to be calming. Therefore, when offering music to a critically ill patient, one should not just turn on the patient's bedside radio leaving this patient unable to control the selection and volume of the music. Chlan also warns against the use of music that is commercially advertised as relaxing as these selections may not be relaxing for all patients. Finally, she warns against the use of free-field music since the music might be irritating to certain patients, family members, and staff in the critical care environment. Chlan and Heiderscheit have developed a music assessment intervention tool for use with mechanically ventilated patients (Chlan 2009). They recommend that a music therapist is involved with the assessment of patient music preferences. If a hospital does not have a music therapist on staff, Chlan (Chlan 2000) recommends that the hospital consults with a music therapist for the implementation of music listening interventions with critically ill patients. More controlled trials are needed with medical patients to further examine which musical characteristics enhance the psychological and physiological benefits from music listening.

We found evidence for reduction of systolic blood pressure but not diastolic blood pressure or mean arterial pressure. These findings may point to the complex physiology underlying haemodynamic responses in critically ill patients requiring ventilator support (Duke 1999).

It is important to note that only one study in this review used a trained music therapist (Phillips 2007). Music therapists in medical settings do not limit their interventions to offering music listening for relaxation purposes. Music therapists are specially trained clinically and academically to carefully assess individual patients' needs, select from a range of music interventions, and use both music and their relationship with patients to offer emotional and spiritual support, enhance sense of control, improve physical well-being, and provide moment-to-moment interactions based on patients' physiological and emotional responses. Because of the lack of randomized controlled trials examining the effect of music therapy interventions on mechanically ventilated patients, it is impossible to establish at this time whether these interventions are more effective than listening to pre-recorded music.

It is recommended that music therapists collaborate with medical personnel in this setting to carefully assess and evaluate the complexity of physiological responses in these patients. Vice versa, it is important that medical personnel providing music experiences to intensive care unit (ICU) patients consult with a music therapist to understand the differential impact of specific music parameters on relaxation responses as well as to perform an accurate assessment of patients' musical preferences. The study by Chlan in this review (Chlan 2013) discusses the role of the music therapist in the assessment of the patients' music preferences.

Implications for research

This systematic review provides evidence that listening to music may have beneficial effects on anxiety in mechanically ventilated patients. All studies but one (Phillips 2007) used pre-recorded music and were carried out by medical professionals. Randomized controlled trials on the use of music therapy (provided by a trained music therapist) with this population are urgently needed. Although the use of pre-recorded music may be preferred by researchers as a standardized stimulus, it is possible to develop music therapy protocols that will allow for individualization according to patient needs while still adhering to randomized controlled trial research standards. Music therapists are urged to formalize protocols to test the effectiveness of their interventions through randomized controlled trials (RCTs).

One should also not ignore the importance of qualitative research and non-randomized controlled trial research to gain a better understanding of the qualitative aspects of the patient's experience and to identify factors that may contribute to or limit the effectiveness of music medicine and music therapy interventions.

The selection of music needs to be carefully considered in future trials. Several studies in this review reported that some participants disliked the music, even though various music styles had been offered to the patients (Lee 2005; Wong 2001). Dislike for the music may agitate the patient and result in an increased stress response. We recommend that researchers use the music preference assessment tool developed by Chlan and Heiderscheit (Chlan 2009) in future trials.

More information is needed about dosages as well as timing of music interventions. We need more studies that examine the relationship between the frequency, duration, and timing of music interventions and treatment effects. Are there optimal lengths of music interventions? Do multiple sessions lead to better results? Are there preferred times during the day to optimize the benefits of music listening? The study by Chlan and colleagues (Chlan 2013) is an excellent example of how some of these questions can be examined. Furthermore, several authors recommended that future studies exert better control over the confounding effects of medication intake on physiological responses (Chlan 1995; Chlan 1997; Chlan 2007a; Lee 2005). When researching critically ill patients, it is not possible to exclude the use of cardiovascular, sedative, and other medications. However, medication intake can be carefully monitored and included as a covariate in the analyses. In addition, future studies should continue to examine the effects of music listening on medication intake. Only three studies (Beaulieu-Boire 2013; Chlan 2013; Conrad 2007) examined the impact of music listening on sedative and analgesic drug intake. Finally, Chlan (Chlan 1997) recommended that future research explore possible interaction effects between music interventions and certain types of medication (for example, sedatives).

One author (Lee 2005) recommended that future studies exclude patients that are on a synchronized intermittent mandatory ventilation (SIMV) ventilator mode. In this mode, the ventilator delivers a mandatory breath to patients when their respiration becomes too slow. Therefore, the breath rate may not accurately reflect the effects of the music when this ventilator mode is used.

Selection of an appropriate measurement tool for anxiety is a major challenge in research studies with mechanically ventilated patients because these patients easily fatigue and have communication limitations. In addition, existing instruments may contain items that lack relevance for this particular population (Chlan 2003). Two authors (Chlan 1997; Lee 2005) reported difficulties with the use of the STAI Short Form (Marteau 1992). Chlan reported a low internal consistency (α = 0.67) and questioned the reliability of this instrument to measure state anxiety in mechanically ventilated patients. Lee, on the other hand, reported that several of the participants had trouble understanding and answering some of the items of the Chinese version of this STAI Short Form. Chlan pointed out that the 6-item STAI scale (Marteau 1992) had not been tested previously with critically ill patients. In 2003, Chlan and colleagues developed a 6-item short form from the STAI with mechanically ventilated patients. This shortened version had good psychometric properties but additional research is needed to further validate this scale (Chlan 2003). Studies included in the update used the Visual Analogue Scale - Anxiety (VAS-A) to measure state anxiety, except for Han (Han 2010) who used the Chinese version of STAI. Chlan (Chlan 2013) reported that concurrent validity between the VAS-A and the STAI has been established. Therefore, researchers should consider using this one-item measurement tool to assess anxiety in mechanically ventilated patients.

Future studies need to include important outcomes such as quality of life, patient satisfaction, time-compression, number of ventilator-dependent days, length of ICU stay, post-discharge outcomes, mortality, and cost-effectiveness assessments. In addition, future studies need to continue to include stress hormone levels as these may provide more sensitive measures of effect and may provide insight into the underlying physiology of anxiety and stress reduction.

Finally, researchers of future studies need to take greater care to design trials that meet current methodological standards (Bradt

2012) and adhere to CONSORT standards for reporting of RCTs (Schulz 2010) including detailing the randomization method, procedures for allocation concealment, blinding of personnel and outcome assessors, and attrition rate and reasons. Although blinding of participants is often not feasible in music medicine or music therapy trials, it is important that future trials meet those design aspects that minimize risk of bias.

Finally, future studies need to include power analyses so that sufficiently large samples are used.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Beaulieu-Boire 2013

Methods	Cross-over design
Participants	Adults with diseases necessitating at least 3 days of invasive mechanical ventilation Diagnoses: respiratory (n = 20), cardiovascular (n = 20), neurological (n = 3), other (n = 6) Average length of mechanical ventilation before onset of study: group A: 11 days (8 to 17); group B: 12 days (6 to 30) Ventilator mode: self-triggering mode Type of airway: not reported N randomized: 55 N analysed: 49 Sex: 17 F, 32 M Age: 62 (3) y Ethnicity: not reported Setting: critical care unit Country: Canada
Interventions	Two study conditions: 1. music condition: listening to music via headphones of an MP3 player 2. placebo sham condition: wearing headphones of an MP3 player with nothing (no music) playing Music selections provided: Bach (Air from Suite for Orchestra No. 3, Bach (Air for G string), Beethoven (Moonlight Sonata), Beethoven (Pathetic Sonata), Brahms (Lullaby), Chopin (Nocturne in G), Debussy (Clair de Lune), Pachelbel (Canon in D), St-Saens (The Swan), Tchaïkovsky (Panorama from Sleeping Beauty) Number of sessions: 4 (2 music, 2 sham) Length of session: 60 minutes Categorized as music medicine study
Outcomes	Sedative drug intake (fentanyl, benzodiazepines, hypnotic propofol): post-test scores Heart rate (HR), respiratory rate (RR), arterial pressure (AP): cannot be included in meta-analysis since means and standard deviations (SD) are not reported Information was requested from the authors but was not received Blood cortisol: change scores Blood ACTH/cortisol ratio: change scores Blood prolactin: post-test scores Blood leptin: post-test scores IL-6: post-test scores C-reactive protein (CRP): no statistical information methionine-enkephalin content (MET-enkephalin): post-test scores
Notes	

Risk of bias

Beaulieu-Boire 2013 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A computer-generated block randomization list was prepared by the investigators" (p. 443)
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was concealed using numbered, opaque sealed envelopes and was revealed by an ICU staff member not involved in the direct care of the randomized patient". (p. 443)
Blinding (performance bias and detection bias) Objective outcomes	Low risk	Blinding of participants was not possible. Staff who administered music or sham were aware of group assignment but these staff were not involved in direct care of the participant
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Each apparatus [MP3 player] was blinded such that the nurse committed in sedative drug tapering was unable to perceive in which group the patient belonged to" (p.444)
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	No subjective outcomes were included in this study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition rate: 10.9%. Quote: "Of the 55 randomized patients, 6 patients did not complete all of the requirements of the protocol (missing listening sessions, missing blood samples, non-completion of the 3-day MV experimental follow-up), and their data were therefore excluded from the analyses" (p. 445)
Selective reporting (reporting bias)	Low risk	No indication of selective reporting
Free from financial conflict of interest	Low risk	Funded by dedicated grants from CRCEL-CHUS (PAFI). This trial is registered in ClinicalTrials.gov: NCT00880035. The authors declare no conflict of interest and they were neither funded to select specific MP3 devices nor to select special music pieces

Chlan 1995

Methods	Two-arm parallel group design
Participants	Adults necessitating mechanical ventilation Diagnoses: pulmonary-related (80%), miscellaneous (20%) (e.g., cancer and kidney transplant) Average length of mechanical ventilation before onset of study: control group: 5.4 days; music group 14.5 days (due to one patient in music group with a ventilator length of 72 days) Ventilator mode: not reported Type of airway: not reported N randomized to music group: 11

	N randomized to control group: 9 N analysed in music group: 11 N analysed in control group: 9 Sex: 7 F, 13 M Age: 59.95 y Ethnicity: not reported Setting: critical care units Country: USA
Interventions	Two study groups: 1. Music group: listening to patient-selected music via headphones 2. Control group: non-music, headphone only Music selections provided: classical selections from Music for Relaxation (Helen Bonny) Number of sessions: 1 Length of session: 30 minutes Categorized as music medicine study
Outcomes	Mood (Profile or Mood States): post-test scores Heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure, oxygen saturation, airway pressure: change scores from pre-test to post-test
Notes	No standard deviations were reported for post-test scores. Additional data were obtained from the lead author. Change scores were computed by JB

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Flip of coin (personal communication with principle investigator (PI))
Allocation concealment (selection bias)	Low risk	Achieved through use of flip of coin for each patient after consent was obtained
Blinding (performance bias and detection bias) Objective outcomes	High risk	Blinding of participants was not possible. Personnel were not blinded
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	The outcome assessor was not blinded (personal communication with PI)
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Self-report measures were used for subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No subject loss

Selective reporting (reporting bias)	Low risk	No indication of selective reporting
Free from financial conflict of interest	Low risk	This study was supported in part by a grant, sponsored by the Medtronic Corporation, from the Greater Twin Cities Area Chapter - American Association of Critical Care Nurses

Chlan 1997

Methods	Two-arm parallel group design
Participants	Adults necessitating mechanical ventilation Diagnoses: pulmonary related (68%), cancer (4%), heart transplant (4%), trauma (5%), miscellaneous (19%) Average length of mechanical ventilation before onset of study: 7.39 days (SD 10.39) Most common ventilator mode: Synchronized Intermittent Mandatory Ventilation (SIMV) (70%). Other ventilator modes: pressure support (PS), positive end expiratory pressure (PEEP), continuous positive airway pressure (CPAP), assist/control (A/C) Type of airway: not reported N randomized to music group: 27 N randomized to control group: 27 N analysed in music group: 27 N analysed in control group: 27 Sex: 59% F, 41% M Age: 57.1y Ethnicity: 92.5% white, 5.5% black, and 2% Native American Setting: critical care units Country: USA
Interventions	Two study groups: 1. Music group: listening to patient-selected music via headphones 2. Control group: quiet rest (no music) Music selections provided: classical, new age, country/western, religious, and easy listening Number of sessions: 1 Length of session: 30 minutes Categorized as music medicine study
Outcomes	State anxiety: post-test scores on the Spielberger State Anxiety Inventory (6-item version) Heart rate: post-test scores (at 30 minutes) Respiratory rate: post-test scores (at 30 minutes)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	Quote: "Subjects were randomized using a table of random numbers, to either the control or treatment condition" (p.44)
Allocation concealment (selection bias)	Low risk	Confirmed through personal communication with author
Blinding (performance bias and detection bias) Objective outcomes	High risk	Blinding of participants was not possible. Personnel were not blinded
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Outcome assessors were not blinded (personal communication with PI)
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Self-report measures were used for subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition rate: 7%
Selective reporting (reporting bias)	Low risk	No indication of selective reporting
Free from financial conflict of interest	Low risk	Unfunded study

Chlan 2007a

Methods	Two-arm parallel group design
Participants	Adults receiving mechanical ventilation in critical care unit Diagnoses: pneumonia (5), respiratory failure (2), shortness of breath (1), ventricular tachycardia (1), and ischaemic bowel (1) Average length of mechanical ventilation before onset of study: 14.2 (15) days Ventilator modes: A/C (6), SIMV (2), and pressure-release (2) Type of airway: not reported N randomized to music group: 5 N randomized to control group: 5 N analysed in music group: 5 N analysed in control group: 5 Age: 64.9 (7.8) y Sex: 6 F, 4 M Ethnicity: 90% white, 10% black Setting: critical care unit Country: USA

Interventions	Two study groups: 1. Music group: listening to patient-selected music via headphone 2. Control group: rest quietly without headphones Number of sessions: 1 Length of session: 60 minutes Categorized as music medicine study
Outcomes	Corticotropin, cortisol, epinephrine and norepinephrine blood samples were obtained from central venous catheter at 4 intervals: baseline, 15 minutes after baseline, 30 minutes after baseline, and 60 minutes after baseline Heart rate: at baseline, 15 minutes after baseline, 30 minutes after baseline, and 60 minutes after baseline
Notes	The data of this study cannot be pooled with data from other studies in this review because of several confounding variables that likely impacted the outcomes at post-test: wide variability in mean levels of biomarkers, a very small sample size, administration of intravenous morphine sulphate to 2 control subjects immediately prior to intervention, and 2 subjects in the experimental group needed endotracheal suctioning during the intervention

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Flip of coin (personal communication with PI)
Allocation concealment (selection bias)	Low risk	Achieved through use of flip of coin
Blinding (performance bias and detection bias) Objective outcomes	High risk	Blinding of participants was not possible. Personnel were not blinded
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Outcome assessors were not blinded (personal communication with PI)
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	This study did not include subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No subject loss
Selective reporting (reporting bias)	Unclear risk	No evidence of selective reporting
Free from financial conflict of interest	Low risk	This study was supported in part by a grant-in-aid from the University of Minnesota Graduate School

Chlan 2007a (*Continued*)

		awarded to Dr Linda Chlan and in part by National Science Foundation grant IBN-0112543 awarded to Dr William Engeland

Chlan 2013

Methods	Three-arm parallel group design
Participants	Adults receiving acute mechanical ventilatory support because of respiratory failure or distress Indication for mechanical ventilation: respiratory failure (n = 63, 63, 61, patient-directed music group, noise-cancelling headphones group, usual care group respectively), respiratory distress (n=32, 27, 36), pneumonia (n = 7, 5, 7), respiratory arrest (n = 3, 4, 4), airway protection (n = 2, 5, 4), postoperative (n = 2, 3, 4), COPD (n = 7, 4, 0), hypoxia (n = 2, 3, 2), ARDS (n = 1, 1, 0), tachypnoea (n = 1, 0, 1), cardiac arrest (n = 4, 2, 5), pulmonary edema (n = 1, 0, 0), asthma (n = 0, 0,1), and other or missing (n = 1, 5, 0) Average length of mechanical ventilation before onset of study: patient-directed music group: 4.5 days (0-35); noise-cancelling headphones group: 6.0 days (1-79), and usual care group: 6.0 days (0 to 38) Ventilator mode:not reported Type of airway: not reported N randomized to patient-directed music group: 126 N randomized to noise-cancelling headphones group: 122 N randomized to usual care group: 125 N analysed to music-directed group: 82 for anxiety analysis, 87 for sedation analysis N analysed to noise-cancelling headphones group: 76 for anxiety analysis, 90 for sedation analysis N analysed to usual care group:83 for anxiety analysis, 89 for sedation analysis Sex: 193 F, 180 M Age: 59 Ethnicity: White (86%); other ethnicities not reported Setting: critical care units at 5 hospitals in Minnesota Country: USA
Interventions	Three study groups: 1. Patient-directed music (PDM) group: listening to patient-preferred music through headphones that contained a data logger system to capture each PDM session and total daily music listening time 2. Noise-canceling headphones (NCH) group: participants were encouraged to wear headphones whenever they wanted to block out the ICU noise or have some quiet time 3. Usual care group: received standard ICU care Music selections provided: starter set of 6 CDs were reviewed with the patient by the research nurse to provide for immediate listening upon randomization to the PDM group. The starter set included relaxing music played on piano, harp, guitar, and Native American flute. Within 24 hours of randomization, the music therapist completed a music preference assessment on each PDM patient using a tool designed to assess music preferences of mechanically ventilated patients with a simple yes or no format

	Number of sessions: the use of listening to music or noise-cancelling headphones was patient-directed. Nursing staff were encouraged to offer the music at least twice per shift but they were reminded that the decision to listen to music was determined by the patient Length of session: variable, determined by the patient. Average length of music listening was 79.8 (SD = 126) minutes per day. Average length of wearing noise-cancelling headphones by the NCH group participants was 34 (89.6) minutes per day Categorized as music medicine study
Outcomes	State anxiety (Visual Analogue Scale - Anxiety), daily sedative drug intensity, daily sedative drug dose frequency: change scores compared to usual care group and mixed models analysis results are reported. Means and SDs per measurement point are not reported Extubation rate at end of study Mortality rate Urinary free cortisol (UFC) (from subsample of patients with intact renal function and not receiving medications known to influence cortisol levels (n = 65)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "A computer-generated random numbers list allocated patients to 1 of 3 groups" (p. 2336)
Allocation concealment (selection bias)	Low risk	Quote: "Group assignment was concealed in an opaque envelope" (p. 2336)
Blinding (performance bias and detection bias) Objective outcomes	High risk	Blinding of the participants was not possible. Personnel were not blinded
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Self-report measure was used for the subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	High risk	Attrition rates for the PDM, NCH, and usual care group were 34.9%, 37.7%, and 33.6% respectively for anxiety analysis and 27.7%, 22.9%, and 28% for the sedation analysis. Reasons for attrition were: participants were not able to complete anxiety assessments each day due to fatigue, medical condition, state of sedation, inability or refusal to complete assessments, or were off the unit (p. 2338)

Chlan 2013 *(Continued)*

Selective reporting (reporting bias)	Low risk	No indication of selective reporting
Free from financial conflict of interest	Low risk	This study was funded by grant R01-NR009295 from the National Institutes of Health, National Institute of Nursing Research. The study is registered on clinicaltrials.gov: NCT00440700

Conrad 2007

Methods	Two-arm parallel group design
Participants	Critically ill adults on mechanical ventilation Average length of mechanical ventilation before onset of study: not reported Ventilator modes: not reported Type of airway: not reported N randomized to music group: 5 N randomized to control group: 5 N analysed in music group: 5 N analysed in control group: 5 Sex: 1 F, 9 M Age M: 59.9 y Ethnicity: not reported Setting: critical care unit Country: Germany
Interventions	Two study groups: 1. Music group: listening to researcher-selected music via headphones 2. Control group: no music with headphones Music selection: "slow-moving" Mozart piano sonatas selected based on compositional elements of relaxation, according to the author: KV283, Andante; KV311, Andantino con espressione; KV330, Andante cantabile; KV332, Adagio; KV333, Andante cantabile; KV545, Andante; KV570, Adagio; and KV576, Adagio Number of sessions: 1 Length of session: 60 min
Outcomes	Sedative drug intake, heart rate variability, arterial pressure, serum level of dehydroepiandrosterone (DHEAS), serum concentrations of growth hormone, interleukin-6: for these variables, means and standard error of the mean (SEM) are given for the control group but not for the music group. Only general statements such as "serum levels of dehydroepiandrosterone remained unchanged during the music intervention" are provided for the music group. Exact P values of between-group changes are given for mean arterial pressure, growth hormone, interleukin-6, epinephrine, and DHEAS, but no mean differences are reported Prolactin, norepinephrine, adrenocorticotropic hormone (ACTH), cortisol, prolactin monomer: only P values are given Because of the limited data reporting, results of this study are only discussed in narrative form in this review

Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Alternate assignment (personal communication with PI)
Allocation concealment (selection bias)	High risk	Allocation concealment was not possible because of the use of alternate assignment
Blinding (performance bias and detection bias) Objective outcomes	Low risk	Participants could not be blinded. Nursing staff who performed outcome assessments were blinded as to whether the patient received music via the headphones
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Outcome assessors were blinded (personal communication with PI)
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	This study did not include subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No subject loss
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Free from financial conflict of interest	Low risk	"The authors did not disclose any conflicts of interest" (p. 2709)

Dijkstra 2010

Methods	Two-arm parallel group design
Participants	Adults in ICU who are mechanically ventilated Indications for mechanical ventilation: abdominal surgery (n = 5), pneumonia (n = 4), cardiovascular (n = 3), sepsis (n = 3), heart transplant (n = 1), lung transplant (n = 1), pancreatitis (n = 1), respiratory distress (n = 1), and trauma (n = 1) Average length of mechanical ventilation before onset of study: 24.6 (3 to 137) days Ventilator mode: pressure support ventilation or assisted spontaneous breathing Type of airway: not reported N randomized to music group: 10 N randomized to control group: 10 N analysed in music group: 10 N analysed in control group:10

	Sex: 8 F, 12 M Age: 52.2 (15.3) y Ethnicity: not reported Setting: critical care units Country: the Netherlands
Interventions	Two study groups: 1. Music group: listening to patient-selected music via headphones 2. Control group: bed rest without headphones Music selections provided: participants were asked to select from classical music or easy listening music. The types of music offered were classical (Anton Bruckner: Quintet F-Dur: Adagio and Gustav Mahler: Symphony Nr. 4 G-Dur: Ruhevoll) and easy listening (film music: Vangelis: 1492, songs without vocals were chosen). Both types of music had slow beats and were relaxing Number of sessions: 3 sessions spread over 2 days Length of session: 30 minutes Categorized as music medicine study
Outcomes	HR, RR, AP, SBP, DBP, sedation scores: change scores Mortality
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote:"Twenty subjects were randomly assigned to either the experimental or control group by the researcher who used a manual method (drawing lots)" (p. 1032)
Allocation concealment (selection bias)	High risk	No allocation concealment was used. Lots were drawn by research team member but not in presence of the participant
Blinding (performance bias and detection bias) Objective outcomes	High risk	Blinding of the participants was not possible. Personnel were not blinded
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "During the music intervention or rest periods, data on physiological parameters and sedation scores were recorded by the attending nurse. The nurse was unaware of the background of the study, to limit bias in the registration of parameters and sedation scores
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	This study did not address subjective outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	No participant loss. Missing values are clearly explained by the authors (p. 1034-5)
Selective reporting (reporting bias)	Low risk	No indication of selective reporting
Free from financial conflict of interest	Low risk	Unfunded research study

Han 2010

Methods	Three-arm parallel group design
Participants	Adults necessitating mechanical ventilation through synchronized intermittent mandatory ventilation or pressure control mode, or both Diagnoses: cardiovascular disease (60%), respiratory problems (26%), and digestive system disease (13%) Average length of mechanical ventilation before onset of study: 3.47 (1 to 161) days Ventilator mode: most common type of ventilatory support was the synchronized intermittent mandatory ventilation mode (86.9%) Type of airway: oral endotracheal tube (89.1%), tracheotomy tube (10.9%) N randomized to music group: 44 N randomized to placebo group: 44 N randomized to control group: 49 N analysed in music group: 44 N analysed in placebo group: 44 N analysed in control group: 49 Sex: 77 F, 60 M Age: 46.18 y Ethnicity: 100% Chinese Setting: critical care units Country: China
Interventions	Three study groups: 1. Music group: listening to patient-selected music via headphones 2. Placebo group: quiet rest while wearing headphones without music 3. Control group: quiet rest without music Music selections provided: participants were asked to select from investigator's selection. There were over 40 choices from four categories of relaxing music, including Western classical music (e.g. Moonlight Sonata, Appassionata), Western light music (e.g. Brahms Lullaby, Ballade pour Adeline), Chinese traditional music (e.g. Butterfly Lovers, Moonlight of Spring River) and Chinese folk songs with lyrics (e.g. Song of Jasmine, Rhythm of a Running Stream). All the musical options were of a relaxing nature containing slow, flowing rhythms that duplicate pulses of 60 to 80 beats per minute (Chlan 1998, 2000) and were familiar to Chinese people Number of sessions: 1 Length of session: 30 minutes Categorized as music medicine study

Outcomes	State anxiety (STAI - Chinese version), HR, RR, SBP, DBP, $Sa0_2$: change scores	
Notes		

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation was generated from the Randomiser website of the Social Psychology Network (1997)" (p. 980)
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) Objective outcomes	High risk	Personnel were not blinded. Authors write that "participants were unaware about the design of the study and the groups assigned to them" (p. 980)
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Quote: "The researcher remained in the room to record the physiological measures across the three groups during the procedure" (p.980). The researcher knew whether participants were listening to music or not
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Self-report measure was used for subjective outcome
Incomplete outcome data (attrition bias) All outcomes	Low risk	No participant loss
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Free from financial conflict of interest	Low risk	This research was funded by the Special Departmental Research Grant from the School of Nursing, The Hong Kong Polytechnic University

Jaber 2007

Methods	Cross-over trial
Participants	Adults on mechanical ventilation Diagnoses: post-surgical (9), pancreatitis (2), respiratory issues (2), sepsis (2) Average length of mechanical ventilation before onset of study: not reported Ventilator mode: not reported Type of airway: oral endotracheal tube (87%), tracheostomy (13%) N analysed in music condition: 15 (ventilated patients only - see notes) N analysed in control condition: 15 (ventilated patients only - see notes)

	Age: 58 (7.8) y Sex: 7 F, 8 M Ethnicity: not reported Setting: critical care unit Country: France
Interventions	Two conditions: 1. Music group: listening to patient-selected music via headphone 2. Control group: uninterrupted rest without music Music selection used: a compilation of patient-preferred music was made by a music therapist according to the following tempo guidelines: the music started at 90 to 100 beats per minute (bpm), then slowed down to 50-60 bpm. The last 5 minutes, the tempo was increased to 70 to 80 bpm to re-energize the patient The music therapist did not implement the music intervention sessions Number of sessions: 1 Length of session: 20 minutes Categorized as music medicine study
Outcomes	Heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure: at 15 minute intervals Because the music selections followed a U-curve (decreasing the tempo and then increasing during the last 5 minutes to re-energize the patient), the data of the 15-minute interval was used The study report does not include standard deviations and precise data for each group. This information was obtained from the lead author
Notes	This study compared ventilated patients (n = 15) with non-ventilated patients (n = 15) . All patients were randomized to receive music listening followed by a period of rest or to first receive a period of rest followed by a period of music. Only data of the ventilated patients were used in this review. Group-specific data were obtained from the author

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Table of random numbers (personal communication with PI)
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) Objective outcomes	High risk	Blinding of the participants was not possible. Personnel were not blinded
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Outcome assessors were blinded to treatment (personal communication with author)

Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	This study did not include subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition rate for entire study sample (see notes) was 14%.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Free from financial conflict of interest	Unclear risk	Funding information is not provided. Conflict of interest statement is lacking

Korhan 2011

Methods	Two-arm parallel group design
Participants	Adults in ICU receiving mechanical ventilation Average length of mechanical ventilation before onset of study: 8.32 (SD = 1.37) days within a range of 1 to 30 days Medical diagnoses: pulmonary (n = 25), heart failure (n = 21), chronic kidney failure (n = 5), pancreatitis (n = 4) and liver failure (n = 5) Ventilator mode: positive end-expiratory pressure Type of airway: not reported N randomized to music group: 30 N randomized to control group:30 N analysed in music group: not reported N analysed in control group:not reported Sex: 28 F, 32 M Age: 45.31 y Ethnicity: 100% Turkish Setting: critical care units Country: Turkey
Interventions	Two study groups: 1. Music group: listening to researcher-selected music via headphones 2. Control group: standard care group Music selections provided: Bach's 19 trio sonatas played by James Galway on flute, 60 to 66 beats per minute Number of sessions: 1 Length of session: 60 minutes Categorized as music medicine study
Outcomes	HR, RR, SBP, DBP, SaO_2: only P values and visual graphs are reported. We contacted the authors to obtain means and SDs but no reply was received
Notes	
Risk of bias	

Korhan 2011 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported. We contacted the authors for additional information but no reply was received
Allocation concealment (selection bias)	Unclear risk	Not reported. We contacted the authors for additional information but no reply was received
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not reported. We contacted the authors for additional information but no reply was received
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Quote: "The research nurse was not blinded as to the allocation of each group" (p.1033). All physiological responses were recorded from a monitoring device by the research nurse
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	This study did not include subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported. We contacted the authors for additional information but no reply was received
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Free from financial conflict of interest	Low risk	This study was funded by Ege University Research Foundation

Lee 2005

Methods	Two-arm parallel group design
Participants	Adults on mechanical ventilation Diagnoses: respiratory problems (39%) and postoperative surgical problems (34.3%) Average length of mechanical ventilation before onset of study: 2.5 (3.3) days Most frequently used ventilator mode: pressure support (PS) (89%) Most common type of airway: oral endotracheal tube (91%). Other: nasal (4%) and tracheostomy (4%) Ethnicity: Chinese N randomized to music group: unclear N randomized to control group: unclear N analysed in music group: 32 N analysed in control group: 32 Sex: 18 F, 46 M Age: 69.4 y Ethnicity: 100% Chinese

	Setting: critical care unit Country: China
Interventions	Two study groups: 1. Music group: listening to patient-selected music via headphones 2. Control group: quiet rest with headphones Music selections provided: Chinese classical music, religious music (Buddhist and Christian), Western classical music and music with "natural sounds" Number of sessions: 1 Length of session: 30 minutes Categorized as music medicine study
Outcomes	State anxiety: change scores from pre-test to post-test on the Spielberger State Anxiety Inventory (6-item version) Heart rate: change scores from pre-test to post-test Respiratory rate: change scores from pre-test to post-test Systolic blood pressure: change scores from pre-test to post-test Diastolic blood pressure: change scores from pre-test to post-test
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Subjects were randomly assigned to either experimental or control group by having a case nurse draw lots" (p. 613)
Allocation concealment (selection bias)	Low risk	Achieved through use of draw of lots by independent group assigner after consent was obtained
Blinding (performance bias and detection bias) Objective outcomes	Low risk	Participants could not be blinded. Personnel were blinded
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The researcher was blind to the treatment condition of both groups during the whole period of data collection" (p. 614)
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Self-report measure was used for subjective outcome
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is unclear whether number of participants analysed equals the number of participants recruited
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting

Free from financial conflict of interest	Unclear risk	Funding information is not provided. Conflict of interest statement is lacking

Phillips 2007

Methods	Randomized controlled trial Randomization method: alternate assignment Allocation concealment: inadequate Blinding: unclear Design: repeated measures control group design Intention to treat: adequate
Participants	Adults with various diagnoses on mechanical ventilation: cardiac problems (56%), pulmonary issues (21%), traumatic injury (8%), other (15%) Average length of mechanical ventilation before onset of study: not reported Ventilator mode: not reported Type of airway: no tracheostomy N randomized to music group (medical): 10 N randomized to music group (cardiac): 10 N randomized to control group (medical): 10 N randomized to control group (cardiac): 10 N analysed in music group (medical): 10 N analysed in music group (cardiac): 9 (not included in this review) N analysed in control group (medical): 10 N analysed in control group (cardiac): 10 (not included in this review) Sex: 10 F, 10 M (for medical, non-cardiac patients) Age: 57.5 y Ethnicity: not reported Setting: critical care unit Country: USA
Interventions	Two study groups: 1. Music group: music therapy entrainment intervention, matching live music to respiratory rate of patients 2. Control group: quiet rest only Patient-selected live music used. Music therapist used guitar and voice Number of sessions: 1 Length of session: 25 minutes Categorized as music therapy study
Outcomes	Hear rate: change scores from pre-test to post-test Respiratory rate: change scores from pre-test to post-test Oxygen saturation level: change scores from pre-test to post-test Rapid shallow breathing: change scores from pre-test to post-test
Notes	Only the data of the medical, non-cardiac patients are included in this review. The cardiac patients were treated immediately following cardiac artery bypass grafting surgery and their physiological responses were still suppressed by the anaesthesia

	The SDs reported in this study are large. Large SDs were present at baseline, meaning that there was a large variety in physiological responses even before the start of the intervention. The author did not report standard deviations (SDs) for the reported change score so we computed these. Since we did not have information about the correlation coefficient, we used a conservative estimate of 0.5. This made the SD of the change score large (i.e., similar to SDs of pre- and post-test scores)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Alternate group assignment
Allocation concealment (selection bias)	High risk	Allocation concealment was not possible because of use of alternate group assignment
Blinding (performance bias and detection bias) Objective outcomes	High risk	Participants could not be blinded. Personnel were blinded
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	This study does not include subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition rate: 0%
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Free from financial conflict of interest	Low risk	Unfunded study (Master's thesis)

Wong 2001

Methods	Cross-over trial
Participants	Adults receiving mechanical ventilation in critical care unit Most frequent primary diagnosis: pulmonary disease (no further details reported) Average length of mechanical ventilation before onset of study: 6.05 (3.65) days Ventilator mode: PS (80%), SIMV + PS (20%) Type of airway: tracheostomy (60%), oral endotracheal tube (40%) Diagnosis: pulmonary diseases N randomized to music group: unclear

	N randomized to control group: unclear N analysed in music condition: 20 N analysed in control condition: 20 Age: 58.25 y Sex: 5 F, 15 M Ethnicity: Chinese Setting: inpatient critical care unit Country: China
Interventions	Two study groups: 1. Music group: listening to patient-selected music via headphone 2. Control group: uninterrupted rest Music selection used: Chinese music (Chinese folk song, music played by Chinese instruments, Chinese music played by Western instruments, Buddhist music) and various Western music (classical, soundtrack, piano) Number of sessions: each subject participated in one music condition and one rest condition Length of condition: 30 minutes Categorized as music medicine study
Outcomes	State anxiety (short form; data was converted to full score): post-test score on the Spielberger State Anxiety Inventory (6-item version) Respiratory rate: post-test score Mean blood pressure: post-test score
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Randomization to different orderings of the interventions was done by drawing lots [...]" (p. 379)
Allocation concealment (selection bias)	Low risk	Achieved through use of draw of lots for each patient after consent was obtained
Blinding (performance bias and detection bias) Objective outcomes	High risk	Participants could not be blinded. Personnel were blinded
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Outcome assessor was not blinded
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Self-report measures were used for subjective outcomes

Wong 2001 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is unclear whether number of participants analysed equals the number of participants recruited
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Free from financial conflict of interest	Unclear risk	Funding information is not provided. Conflict of interest statement is lacking

Wu 2008

Methods	Two-arm parallel group design
Participants	Adults necessitating mechanical ventilation Participants were suffering from lung-related diseases (n = 39) and non-lung related diseases (n = 21) Average length of mechanical ventilation before onset of study: 3.47 (1 to 161) days Ventilator mode: not reported Type of airway: oral endotracheal tube and tracheotomy tube N randomized to music group: 30 N randomized to control group: 30 N analysed in music group: 30 N analysed in control group: 30 Sex: 23 F, 37 M Age: mean age not reported Ethnicity: 100% Chinese Setting: critical care unit Country: Taiwan
Interventions	Two study groups: 1. Music group: music listening via headphones 2. Control group: quiet rest without music Music selections provided: participants were asked to select from Chinese, religious, New Age, hymn, classical or orchestral music with slow tempo. Most participants selected old Taiwanese popular songs without lyrics (n = 17) and religious music (n = 7, 24) Number of sessions: 1 Length of session: 30 minutes Categorized as music medicine study
Outcomes	Anxiety (VAAS): change scores HR, RR, SBP, DBP, MAP, O_2sa: change scores
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Wu 2008 *(Continued)*

Random sequence generation (selection bias)	Low risk	Use of coin flip
Allocation concealment (selection bias)	Low risk	Use of coin flip
Blinding (performance bias and detection bias) Objective outcomes	High risk	Blinding of the participants was not possible. Personnel were not blinded
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Outcome assessors were not blinded
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Self-report measures were used for subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No participant loss
Selective reporting (reporting bias)	Low risk	No indication of selective reporting
Free from financial conflict of interest	Low risk	Unfunded research study

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Almerud 2003	Insufficient data reporting
Austin 2010	Review article
Bauer 2002	Commentary on Wong 2001
Besel 2006	Not randomized controlled trial (RCT) or controlled clinical trial (CCT)
Burke 1995	Not RCT or CCT
Caine 1991	Not population of interest
Chlan 2000	Programme description
Chlan 2001	Not RCT or CCT
Chlan 2006	Not RCT or CCT

(*Continued*)

Chlan 2011	Not RCT or CCT. Report on analysis of anxiety patterns of subsample of the 2013 RCT included in this review
Chou 2003	Not RCT or CCT
Davis 2012	review article
Fontaine 1994	Programme description
Hansen-Flachen 1994	Not RCT or CCT
Ho 2012	Review article
Hunter 2010	Not RCT or CCT
Iriarte 2003	Not RCT or CCT
Lorch 1994	Not population of interest
Nilsson 2011	Commentary on Bradt 2010
Standley 1995	Not population of interest
Tate 2010	Not population of interest
Twiss 2006	Not randomized controlled trial. In the thesis author explicitly states that only 4 CD players were available. If all CD players were in use, the next group of patients were placed in the control group
Wiens 1995	Not population of interest

DATA AND ANALYSES

Comparison 1. Music versus standard care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 State Anxiety (change scores)	5	288	Std. Mean Difference (IV, Random, 95% CI)	-1.11 [-1.75, -0.47]
2 Heart Rate	8	338	Mean Difference (IV, Random, 95% CI)	-3.95 [-6.62, -1.27]
2.1 Final score	2	63	Mean Difference (IV, Random, 95% CI)	-5.26 [-13.56, 3.03]
2.2 Change score	6	275	Mean Difference (IV, Random, 95% CI)	-3.82 [-6.83, -0.82]
3 Heart Rate (adequate randomization)	7	318	Mean Difference (IV, Random, 95% CI)	-4.01 [-6.80, -1.22]
4 Respiratory Rate	9	357	Mean Difference (IV, Random, 95% CI)	-2.87 [-3.64, -2.10]
4.1 Final score	3	83	Mean Difference (IV, Random, 95% CI)	-2.14 [-4.06, -0.22]
4.2 Change score	6	274	Mean Difference (IV, Random, 95% CI)	-3.01 [-3.85, -2.17]
5 Respiratory Rate (adequate randomization)	8	337	Mean Difference (IV, Random, 95% CI)	-2.87 [-3.64, -2.09]
6 Systolic Blood Pressure	6	269	Mean Difference (IV, Random, 95% CI)	-4.22 [-6.38, -2.06]
6.1 Final score	1	14	Mean Difference (IV, Random, 95% CI)	-9.0 [-22.40, 4.40]
6.2 Change score	5	255	Mean Difference (IV, Random, 95% CI)	-4.09 [-6.28, -1.90]
7 Diastolic Blood Pressure	6	269	Mean Difference (IV, Random, 95% CI)	-2.16 [-4.40, 0.07]
7.1 Final score	1	14	Mean Difference (IV, Random, 95% CI)	-3.70 [-15.17, 7.77]
7.2 Change score	5	255	Mean Difference (IV, Random, 95% CI)	-2.13 [-4.58, 0.31]
8 Mean Arterial Pressure	3	98	Mean Difference (IV, Random, 95% CI)	-1.79 [-4.56, 0.99]
8.1 Final score	1	20	Mean Difference (IV, Random, 95% CI)	-4.75 [-17.81, 8.31]
8.2 Change score	2	78	Mean Difference (IV, Random, 95% CI)	-1.65 [-4.49, 1.20]
9 Oxygen Saturation Level (change scores)	4	193	Mean Difference (IV, Random, 95% CI)	-0.05 [-0.67, 0.57]
10 Mortality	2	271	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.38, 1.51]

Analysis 1.1. Comparison 1 Music versus standard care, Outcome 1 State Anxiety (change scores).

Review: Music interventions for mechanically ventilated patients

Comparison: 1 Music versus standard care

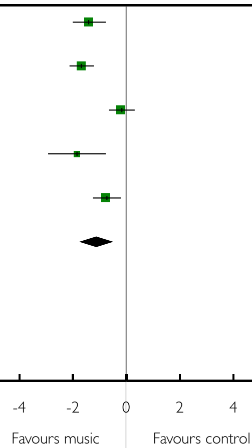
Outcome: 1 State Anxiety (change scores)

Study or subgroup	Music N	Music Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Chlan 1997	24	-7.17 (3.85)	27	-1.55 (4.08)		20.3 %	-1.39 [-2.01, -0.77]
Han 2010	44	-10.7 (6.82)	49	-0.76 (4.97)		22.0 %	-1.67 [-2.14, -1.19]
Lee 2005	32	-1.6 (3.81)	32	-1 (3.31)		21.8 %	-0.17 [-0.66, 0.32]
Wong 2001	10	-14 (5.62)	10	-3.84 (4.97)		14.5 %	-1.83 [-2.92, -0.75]
Wu 2008	30	-4.43 (7.19)	30	0.83 (6.88)		21.4 %	-0.74 [-1.26, -0.21]
Total (95% CI)	**140**		**148**			**100.0 %**	**-1.11 [-1.75, -0.47]**

Heterogeneity: $Tau^2 = 0.42$; $Chi^2 = 23.42$, df = 4 (P = 0.00010); $I^2 = 83\%$

Test for overall effect: Z = 3.42 (P = 0.00063)

Test for subgroup differences: Not applicable



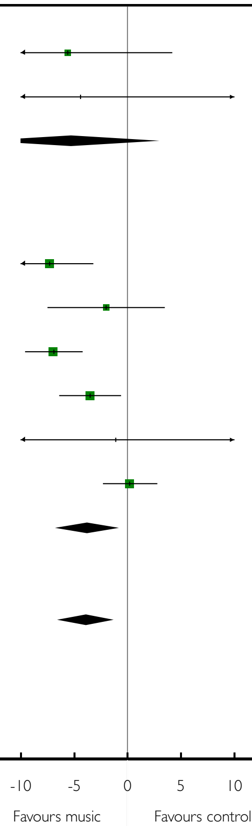
Analysis 1.2. Comparison 1 Music versus standard care, Outcome 2 Heart Rate.

Review: Music interventions for mechanically ventilated patients

Comparison: 1 Music versus standard care

Outcome: 2 Heart Rate

Study or subgroup	Music N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Final score							
Chlan 1997	26	85.9 (15.6)	23	91.5 (18.9)		5.8 %	-5.60 [-15.38, 4.18]
Jaber 2007	7	84.7 (15)	7	89.1 (14.9)		2.6 %	-4.40 [-20.06, 11.26]
Subtotal (95% CI)	**33**		**30**			**8.4 %**	**-5.26 [-13.56, 3.03]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.02, df = 1 (P = 0.90); I^2 =0.0%							
Test for overall effect: Z = 1.24 (P = 0.21)							
2 Change score							
Chlan 1995	11	-8.9 (5.56)	9	-1.6 (3.63)		16.1 %	-7.30 [-11.35, -3.25]
Dijkstra 2010	8	-1.6 (3.3)	10	0.4 (8)		12.4 %	-2.00 [-7.46, 3.46]
Han 2010	44	-5.59 (7.3)	49	1.33 (5.61)		20.4 %	-6.92 [-9.59, -4.25]
Lee 2005	32	-3.8 (7)	32	-0.3 (4.4)		19.8 %	-3.50 [-6.36, -0.64]
Phillips 2007	10	0.2 (24.69)	10	1.3 (15.77)		2.0 %	-1.10 [-19.26, 17.06]
Wu 2008	30	-0.93 (5.79)	30	-1.17 (4.14)		20.8 %	0.24 [-2.31, 2.79]
Subtotal (95% CI)	**135**		**140**			**91.6 %**	**-3.82 [-6.83, -0.82]**
Heterogeneity: Tau^2 = 8.84; Chi^2 = 18.28, df = 5 (P = 0.003); I^2 =73%							
Test for overall effect: Z = 2.50 (P = 0.012)							
Total (95% CI)	**168**		**170**			**100.0 %**	**-3.95 [-6.62, -1.27]**
Heterogeneity: Tau^2 = 7.29; Chi^2 = 18.44, df = 7 (P = 0.01); I^2 =62%							
Test for overall effect: Z = 2.89 (P = 0.0039)							
Test for subgroup differences: Chi^2 = 0.10, df = 1 (P = 0.75), I^2 =0.0%							



Analysis 1.3. Comparison 1 Music versus standard care, Outcome 3 Heart Rate (adequate randomization).

Review: Music interventions for mechanically ventilated patients

Comparison: 1 Music versus standard care

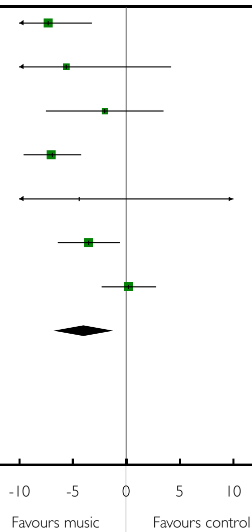
Outcome: 3 Heart Rate (adequate randomization)

Study or subgroup	Music N	Music Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Chlan 1995	11	-8.9 (5.56)	9	-1.6 (3.63)		16.5 %	-7.30 [-11.35, -3.25]
Chlan 1997	26	85.9 (15.6)	23	91.5 (18.9)		6.2 %	-5.60 [-15.38, 4.18]
Dijkstra 2010	8	-1.6 (3.3)	10	0.4 (8)		12.9 %	-2.00 [-7.46, 3.46]
Han 2010	44	-5.59 (7.3)	49	1.33 (5.61)		20.6 %	-6.92 [-9.59, -4.25]
Jaber 2007	7	84.7 (15)	7	89.1 (14.9)		2.8 %	-4.40 [-20.06, 11.26]
Lee 2005	32	-3.8 (7)	32	-0.3 (4.4)		20.0 %	-3.50 [-6.36, -0.64]
Wu 2008	30	-0.93 (5.79)	30	-1.17 (4.14)		21.0 %	0.24 [-2.31, 2.79]
Total (95% CI)	**158**		**160**			**100.0 %**	**-4.01 [-6.80, -1.22]**

Heterogeneity: $Tau^2 = 7.95$; $Chi^2 = 18.36$, df = 6 (P = 0.01); $I^2 = 67\%$

Test for overall effect: Z = 2.82 (P = 0.0048)

Test for subgroup differences: Not applicable



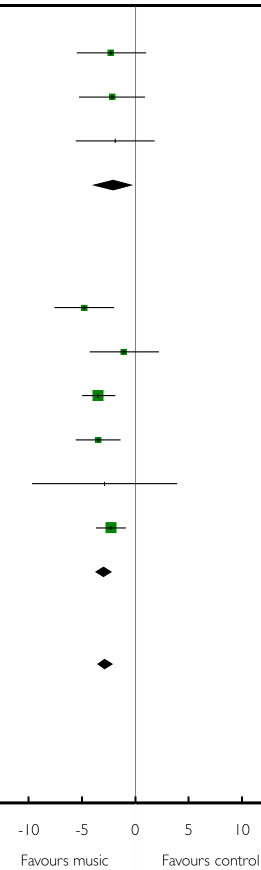
Analysis 1.4. Comparison 1 Music versus standard care, Outcome 4 Respiratory Rate.

Review: Music interventions for mechanically ventilated patients

Comparison: 1 Music versus standard care

Outcome: 4 Respiratory Rate

Study or subgroup	Music N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Final score							
Chlan 1997	23	16.4 (5.5)	26	18.7 (6.1)		5.6 %	-2.30 [-5.55, 0.95]
Jaber 2007	7	23.73 (3.22)	7	25.9 (2.7)		6.1 %	-2.17 [-5.28, 0.94]
Wong 2001	10	17.35 (4.16)	10	19.25 (4.23)		4.4 %	-1.90 [-5.58, 1.78]
Subtotal (95% CI)	**40**		**43**			**16.2 %**	**-2.14 [-4.06, -0.22]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.03, df = 2 (P = 0.99); I^2 =0.0%							
Test for overall effect: Z = 2.19 (P = 0.029)							
2 Change score							
Chlan 1995	11	-5 (3.8)	9	-0.2 (2.45)		7.8 %	-4.80 [-7.56, -2.04]
Dijkstra 2010	8	-1.5 (2.8)	9	-0.4 (4)		5.6 %	-1.10 [-4.35, 2.15]
Han 2010	44	-2.77 (3.64)	49	0.69 (3.93)		25.1 %	-3.46 [-5.00, -1.92]
Lee 2005	32	-3.6 (4.9)	32	-0.1 (3.4)		13.9 %	-3.50 [-5.57, -1.43]
Phillips 2007	10	-0.2 (7.6)	10	2.7 (7.9)		1.3 %	-2.90 [-9.69, 3.89]
Wu 2008	30	-2.7 (3.05)	30	-0.4 (2.48)		30.1 %	-2.30 [-3.71, -0.89]
Subtotal (95% CI)	**135**		**139**			**83.8 %**	**-3.01 [-3.85, -2.17]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 4.47, df = 5 (P = 0.48); I^2 =0.0%							
Test for overall effect: Z = 7.00 (P < 0.00001)							
Total (95% CI)	**175**		**182**			**100.0 %**	**-2.87 [-3.64, -2.10]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 5.15, df = 8 (P = 0.74); I^2 =0.0%							
Test for overall effect: Z = 7.29 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 0.66, df = 1 (P = 0.42), I^2 =0.0%							



Analysis 1.5. Comparison 1 Music versus standard care, Outcome 5 Respiratory Rate (adequate randomization).

Review: Music interventions for mechanically ventilated patients

Comparison: 1 Music versus standard care

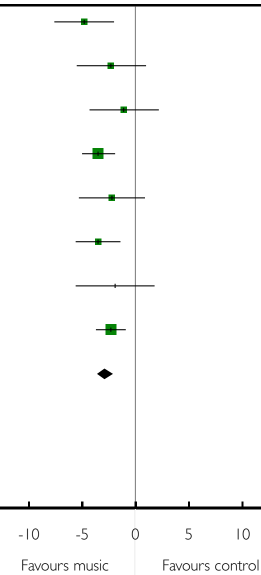
Outcome: 5 Respiratory Rate (adequate randomization)

Study or subgroup	Music N	Music Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Chlan 1995	11	-5 (3.8)	9	-0.2 (2.45)		7.9 %	-4.80 [-7.56, -2.04]
Chlan 1997	23	16.4 (5.5)	26	18.7 (6.1)		5.7 %	-2.30 [-5.55, 0.95]
Dijkstra 2010	8	-1.5 (2.8)	9	-0.4 (4)		5.7 %	-1.10 [-4.35, 2.15]
Han 2010	44	-2.77 (3.64)	49	0.69 (3.93)		25.4 %	-3.46 [-5.00, -1.92]
Jaber 2007	7	23.73 (3.22)	7	25.9 (2.7)		6.2 %	-2.17 [-5.28, 0.94]
Lee 2005	32	-3.6 (4.9)	32	-0.1 (3.4)		14.1 %	-3.50 [-5.57, -1.43]
Wong 2001	10	17.35 (4.16)	10	19.25 (4.23)		4.5 %	-1.90 [-5.58, 1.78]
Wu 2008	30	-2.7 (3.05)	30	-0.4 (2.48)		30.4 %	-2.30 [-3.71, -0.89]
Total (95% CI)	**165**		**172**			**100.0 %**	**-2.87 [-3.64, -2.09]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 5.15$, df = 7 (P = 0.64); $I^2 = 0.0\%$

Test for overall effect: Z = 7.24 (P < 0.00001)

Test for subgroup differences: Not applicable



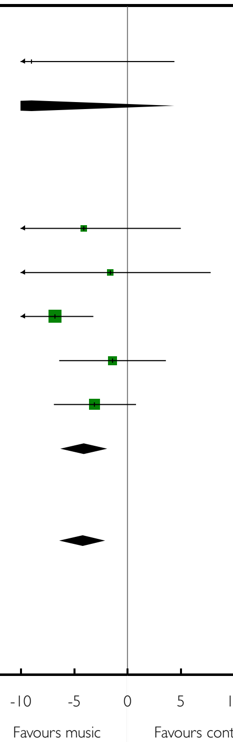
Analysis 1.6. Comparison 1 Music versus standard care, Outcome 6 Systolic Blood Pressure.

Review: Music interventions for mechanically ventilated patients

Comparison: 1 Music versus standard care

Outcome: 6 Systolic Blood Pressure

Study or subgroup	Music N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Final score							
Jaber 2007	7	124.1 (11.2)	7	133.1 (14.2)		2.6 %	-9.00 [-22.40, 4.40]
Subtotal (95% CI)	**7**		**7**			**2.6 %**	**-9.00 [-22.40, 4.40]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.32 (P = 0.19)							
2 Change score							
Chlan 1995	11	-5.1 (12.66)	9	-1 (7.79)		5.7 %	-4.10 [-13.15, 4.95]
Dijkstra 2010	8	-0.4 (8.7)	10	1.2 (11.7)		5.2 %	-1.60 [-11.03, 7.83]
Han 2010	44	-5.23 (9.97)	49	1.53 (7.38)		36.0 %	-6.76 [-10.36, -3.16]
Lee 2005	32	-4.4 (10.6)	32	-3 (9.7)		18.8 %	-1.40 [-6.38, 3.58]
Wu 2008	30	-3.37 (6.73)	30	-0.3 (8.33)		31.7 %	-3.07 [-6.90, 0.76]
Subtotal (95% CI)	**125**		**130**			**97.4 %**	**-4.09 [-6.28, -1.90]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.78$, df = 4 (P = 0.44); $I^2 = 0.0\%$							
Test for overall effect: Z = 3.67 (P = 0.00025)							
Total (95% CI)	**132**		**137**			**100.0 %**	**-4.22 [-6.38, -2.06]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 4.28$, df = 5 (P = 0.51); $I^2 = 0.0\%$							
Test for overall effect: Z = 3.83 (P = 0.00013)							
Test for subgroup differences: $Chi^2 = 0.50$, df = 1 (P = 0.48), $I^2 = 0.0\%$							



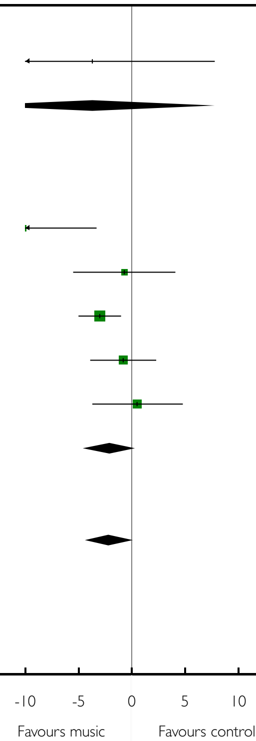
Analysis 1.7. Comparison 1 Music versus standard care, Outcome 7 Diastolic Blood Pressure.

Review: Music interventions for mechanically ventilated patients

Comparison: 1 Music versus standard care

Outcome: 7 Diastolic Blood Pressure

Study or subgroup	Music N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Final score							
Jaber 2007	7	75.1 (10.8)	7	78.8 (11.1)		3.5 %	-3.70 [-15.17, 7.77]
Subtotal (95% CI)	**7**		**7**			**3.5 %**	**-3.70 [-15.17, 7.77]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.63 (P = 0.53)							
2 Change score							
Chlan 1995	11	-8.5 (8.39)	9	1.7 (7.29)		8.5 %	-10.20 [-17.08, -3.32]
Dijkstra 2010	8	1 (5)	10	1.7 (5.3)		14.7 %	-0.70 [-5.47, 4.07]
Han 2010	44	-2.41 (4.79)	49	0.57 (5.15)		32.3 %	-2.98 [-5.00, -0.96]
Lee 2005	32	-3.5 (5.4)	32	-2.7 (7.2)		23.7 %	-0.80 [-3.92, 2.32]
Wu 2008	30	0.37 (7.83)	30	-0.17 (8.77)		17.2 %	0.54 [-3.67, 4.75]
Subtotal (95% CI)	**125**		**130**			**96.5 %**	**-2.13 [-4.58, 0.31]**
Heterogeneity: Tau^2 = 3.86; Chi^2 = 8.56, df = 4 (P = 0.07); I^2 =53%							
Test for overall effect: Z = 1.71 (P = 0.087)							
Total (95% CI)	**132**		**137**			**100.0 %**	**-2.16 [-4.40, 0.07]**
Heterogeneity: Tau^2 = 2.97; Chi^2 = 8.62, df = 5 (P = 0.13); I^2 =42%							
Test for overall effect: Z = 1.89 (P = 0.058)							
Test for subgroup differences: Chi^2 = 0.07, df = 1 (P = 0.79), I^2 =0.0%							



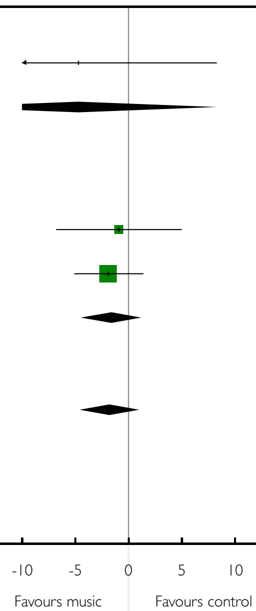
Analysis 1.8. Comparison 1 Music versus standard care, Outcome 8 Mean Arterial Pressure.

Review: Music interventions for mechanically ventilated patients

Comparison: 1 Music versus standard care

Outcome: 8 Mean Arterial Pressure

Study or subgroup	Music N	Music Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Final score							
Wong 2001	10	76.15 (15.37)	10	80.9 (14.41)		4.5 %	-4.75 [-17.81, 8.31]
Subtotal (95% CI)	**10**		**10**			**4.5 %**	**-4.75 [-17.81, 8.31]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.71 (P = 0.48)							
2 Change score							
Dijkstra 2010	8	0.4 (6.4)	10	1.3 (6.3)		22.1 %	-0.90 [-6.81, 5.01]
Wu 2008	30	-2.12 (5.13)	30	-0.25 (7.47)		73.4 %	-1.87 [-5.11, 1.37]
Subtotal (95% CI)	**38**		**40**			**95.5 %**	**-1.65 [-4.49, 1.20]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.08$, df = 1 (P = 0.78); I^2 =0.0%							
Test for overall effect: Z = 1.13 (P = 0.26)							
Total (95% CI)	**48**		**50**			**100.0 %**	**-1.79 [-4.56, 0.99]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.29$, df = 2 (P = 0.87); I^2 =0.0%							
Test for overall effect: Z = 1.26 (P = 0.21)							
Test for subgroup differences: $Chi^2 = 0.21$, df = 1 (P = 0.65), I^2 =0.0%							



Analysis 1.9. Comparison 1 Music versus standard care, Outcome 9 Oxygen Saturation Level (change scores).

Review: Music interventions for mechanically ventilated patients

Comparison: 1 Music versus standard care

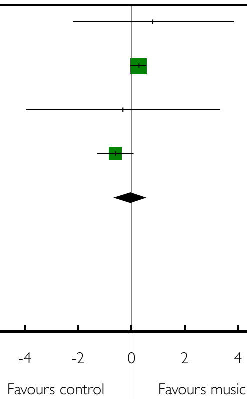
Outcome: 9 Oxygen Saturation Level (change scores)

Study or subgroup	Music N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Chlan 1995	11	0.6 (4.6)	9	-0.2 (2)		4.0 %	0.80 [-2.22, 3.82]
Han 2010	44	0.02 (0.7)	49	-0.24 (0.83)		56.9 %	0.26 [-0.05, 0.57]
Phillips 2007	10	-0.21 (5.46)	10	0.1 (2.17)		2.8 %	-0.31 [-3.95, 3.33]
Wu 2008	30	-0.33 (0.88)	30	0.27 (1.72)		36.4 %	-0.60 [-1.29, 0.09]
Total (95% CI)	**95**		**98**			**100.0 %**	**-0.05 [-0.67, 0.57]**

Heterogeneity: $Tau^2 = 0.15$; $Chi^2 = 5.19$, df = 3 (P = 0.16); $I^2 = 42\%$

Test for overall effect: Z = 0.15 (P = 0.88)

Test for subgroup differences: Not applicable



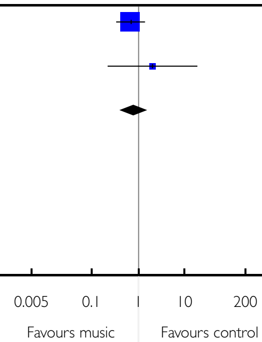
Analysis 1.10. Comparison 1 Music versus standard care, Outcome 10 Mortality.

Review: Music interventions for mechanically ventilated patients

Comparison: 1 Music versus standard care

Outcome: 10 Mortality

Study or subgroup	Music n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Chlan 2013	11/126	16/125		90.4 %	0.68 [0.33, 1.41]
Dijkstra 2010	2/10	1/10		9.6 %	2.00 [0.21, 18.69]
Total (95% CI)	**136**	**135**		**100.0 %**	**0.76 [0.38, 1.51]**



Total events: 13 (Music), 17 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.81$, df = 1 (P = 0.37); $I^2 = 0.0\%$

Test for overall effect: Z = 0.79 (P = 0.43)

Test for subgroup differences: Not applicable

APPENDICES

Appendix 1. MEDLINE search strategy (OvidSP)

1 music/
2 music therapy/
3 (music$ or rhythm$ or melod$).tw.
4 (singing or sing or song$ or compos$ or improvis$).tw.
5 or/1-4
6 Respiration artificial/
7 (artificial adj5 ventil$).tw.
8 (Ventilat$ adj5 mechanical).tw.
9 Intubation, intratracheal/
10 exp respiratory insufficiency/
11 (respiratory failure or (respiratory adj5 failure)).tw.
12 Suction/
13 or/6-12
14 randomized controlled trial.pt.
15 controlled clinical trial.pt.
16 randomized controlled trial.sh.

17 random allocation.sh.
18 double blind method.sh.
19 single blind method.sh.
20 or/14-19
21 (animals not human).sh.
22 20 not 21
23 clinical trial.pt.
24 exp clinical trial/
25 (clin$ adj25 trial$).ti,ab.
26 ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab
27 placebos.sh.
28 placebo$.ti,ab.
29 random$.ti,ab.
30 research design.sh.
31 or/23-30
32 31 not 21
33 22 or 32
34 5 and 13
35 33 and 34

Appendix 2. PsycINFO search strategy (OvidSP)

1. empirical study.md. or followup study.md. or longitudinal study.md. or prospective study.md. or quantitative study.md. or treatment effectiveness evaluation/ or exp hypothesis testing/ or repeated measures/ or exp experimental design/ or placebo$.ti,ab. Or random$.ti,ab. Or (clin$ adj25 trial$).ti,ab. Or ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab
2. artificial respiration/ or artificial near ventil$.tw. or Ventilat$ near mechanical.tw. or exp Trachea/ or intubation.tw. or respiratory failure.mp. or respiratory failure.tw. or suction.mp.
3. (empirical study or followup study or longitudinal study or prospective study or quantitative study).md. or treatment effectiveness evaluation/ or exp hypothesis testing/ or repeated measures/ or exp experimental design/ or placebo$.ti,ab. or random$.ti,ab. or (clin$ adj25 trial$).ti,ab. or ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab.
4. 1 and 2 and 3

Appendix 3. CENTRAL search strategy

#1 MeSH descriptor Music, this term only
#2 MeSH descriptor Music Therapy explode all trees
#3 music* or rhythm* or melod*
#4 singing or sing or song* or compos* or listening or improvis*
#5 (#1 OR #2 OR #3 OR #4)
#6 MeSH descriptor Respiration, Artificial, this term only
#7 artificial near ventil*
#8 Ventilat* near mechanical
#9 MeSH descriptor Intubation, Intratracheal, this term only
#10 MeSH descriptor Respiratory Insufficiency explode all trees
#11 (respiratory failure) or (respiratory near failure)
#12 MeSH descriptor Suction explode all trees
#13 (#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12)
#14 (#5 AND #13)

Appendix 4. EMBASE search strategy (OvidSP)

1 exp MUSIC THERAPY/ or exp MUSIC/
2 (music$ or rhythm$ or melod$).tw.
3 (singing or sing or song$ or compos$ or listening or improvis$).tw.
4 or/1-3
5 Respiration artificial/
6 (artificial adj10 ventilat$).mp.
7 (Ventilat$ adj10 mechanical).tw.
8 exp Endotracheal Intubation/
9 exp Respiratory Failure/
10 respiratory failure.mp. or (respiratory adj10 failure).tw.
11 Suction.mp. or SUCTION/
12 or/5-11
13 4 and 12
14 Randomized Controlled Trial/
15 RANDOMIZATION/
16 Controlled Study/
17 Multicenter Study/
18 Phase 3 Clinical Trial/
19 Phase 4 Clinical Trial/
20 Double Blind Procedure/
21 Single Blind Procedure/
22 (RANDOM* or CROSS?OVER* or FACTORIAL* or PLACEBO* or VOLUNTEER*).ti,ab.
23 ((SINGL* or DOUBL* or TREBL* or TRIPL*) adj5 (BLIND* or MASK*)).ti,ab.
24 or/14-23
25 HUMAN.sh,hw.
26 25 and 24
27 26 and 13

Appendix 5. CINAHL search strategy (EBSCOhost)

S1 TX compos* or TX singing or TX sing or TX song* or TX music* or TX rhythm* or TX melod* or MH music or MH music therapy
S2 (MH “Intubation, Intratracheal”) or (MH “Extubation”) or (MH “Suction”) or (MH “Suctioning, Endotracheal”) or (MH “Airway Suctioning”) or TX ventilator N5 weaning or TX respiratory N5 failure or (respiratory failure) or (MH “Respiratory Failure”) or (MH “Ventilator Weaning”) or TX Ventilat* N5 mechanical or TX artificial N5 ventil* or respiratory insufficiency or (artificial respiration) or (MH “Ventilation, Mechanical+”) or (MH “Ventilators, Mechanical”)
S3 (S1 and S2) not animal*

Appendix 6. LILACS search strategy (Virtual Health Library))

(music$) and ((mechanical and ventilation) or (intratracheal and intubation) or (respiratory and failure) or “RESPIRATORY FAILURE” or (artificial and respiration) or (suction) or (“SUCTION”))

Appendix 7. AMED search strategy (OvidSP)

	Searches
1	Music/
2	Music Therapy/
3	(music$ or rhythm$ or melod$).tw.
4	(singing or sing or song$ or compos$ or listening or improvis$).tw
5	or/1-4
6	Respiration artificial/
7	artificial near ventil$.tw.
8	Ventilat$ near mechanical.tw.
9	exp respiratory insufficiency/
10	respiratory failure.mp. or respiratory near failure.tw. [mp=abstract, heading words, title]
11	exp Intubation/
12	or/6-11
13	5 and 12

Appendix 8. ISI Web of Science search strategy

#1 TS=(Respiration artificial) or TS=(artificial SAME ventil*) or TS=(Ventilat* SAME mechanical) or TS=(Intubation SAME intra-tracheal) or TS=(respiratory insufficiency) or TS=(respiratory SAME failure)
#2 TS=music* or TS=(music therapy) or TS=(singing or song or song* or compos* or improvis* or rhythm* or melod*) or TS=(suction)
#3 TS=(control$ or prospectiv$ or volunteer$) or TS=(prospective studies) or TS=(follow up studies) or TS=(evaluation studies) or TS=(comparative study) or TS=random$ or TS=placebo$ or TS=(Clinical trial$) or TS=(single-blind method$) or TS=(double blind method$) or TS=(randomized controlled trial$) or TS=(controlled clinical trial$) or TS=(random allocation)
#4 #1 and #2 and #3

Appendix 9. The specialist music therapy research database search strategy

Research database is no longer functional. Archives of research reports, dissertations and conference proceedings were handsearched.

Appendix 10. CAIRSS for Music search strategy (Webvoyage)

(“mechanical ventilation”)[in Keyword Anywhere] OR (“artificial ventilation”)[in Keyword Anywhere] OR (“artificial respiration”)[in Keyword Anywhere] (intubation)[in Keyword Anywhere] OR (“suction”)[in Keyword Anywhere] (“respiratory failure” [in Keyword Anywhere] OR (“respiratory insufficiency”)[in Keyword Anywhere]

Appendix 11. Proquest Digital Dissertations search strategy (Proquest)

((artificial) W/3 (respir*)) AND ((Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)) ((artificial) W/3 (ventilation)) AND ((Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)) ((mechanical) W/3 (ventilation)) AND ((Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)) ((intubation or suction)) AND ((Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)) ((respirat*) w/3 (insufficien*)) AND ((Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)) ((respirat*) w/3 (failure*)) AND ((Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*))

Appendix 12. Clinical trials.gov search strategy

(music or “music therapy”)

Appendix 13. Current Controlled Trials search strategy

music
music therapy

Appendix 14. National Research Registry search strategy

music

Appendix 15. NIH CRISP search strategy

music

Appendix 16. Search strategy 2014

Medline search strategy (OvidSP)

1	music/
2	music therapy/
3	(music$ or rhythm$ or melod$).tw.
4	(singing or sing or song$ or compos$ or improvis$).tw.
5	or/1-4
6	Respiration artificial/
7	(artificial adj5 ventil$).tw.
8	(Ventilat$ adj5 mechanical).tw.
9	Intubation, intratracheal/
10	exp respiratory insufficiency/
11	(respiratory failure or (respiratory adj5 failure)).tw.
12	Suction/
13	or/6-12
14	randomized controlled trial.pt.
15	controlled clinical trial.pt.
16	randomized.ab.
17	placebo.ab.
18	drug therapy.fs.
19	randomly.ab.
20	trial.ab.

(*Continued)*

21	groups.ab.
22	or/14-21
23	exp animals/ not humans.sh.
24	22 not 23
25	5 and 13 and 24
26	limit 25 to yr="2010 - 2014"

PsycINFO search strategy (EBSCOhost)

S1 DE music
S2 DE (music therapy)
S3 TX (music* or rhythm* or melod* or singing or sing or song* or compos* or listening or improvis*)
S4 S1 OR S2 OR S3
S5 DE "Artificial Respiration"
S6 TX (artificial N5 ventil*)
S7 TX (Ventilat* N5 mechanical)
S8 DE "Trachea"
S9 TX intubation
S10 TX (respiratory failure)
S11 TX (suction*)
S12 S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11
S13 MR ((empirical study) or (followup study) or (longitudinal study) or (prospective study) or (clinical trial))
S14 DE "Treatment Effectiveness Evaluation"
S15 DE "Experimental Design" OR DE "Between Groups Design" OR DE "Clinical Trials" OR DE "Cohort Analysis" OR DE "Followup Studies" OR DE "Hypothesis Testing" OR DE "Longitudinal Studies" OR DE "Repeated Measures" OR DE "Between Groups Design"
S16 TI(placebo* or random* or randomized* or trial or groups)
S17 AB(placebo* or random* or randomized* or trial or groups)
S18 AB(placebo* or random* or randomized* or trial or groups)
S19 S13 OR S14 OR S15 OR S16 OR S17 OR S18
S20 S4 AND S12 AND S19
S21 S20 Limiters - Publication Year: 2010-2013

CENTRAL search strategy

#1 MeSH descriptor Music, this term only
#2 MeSH descriptor Music Therapy explode all trees
#3 music* or rhythm* or melod*
#4 singing or sing or song* or compos* or listening or improvis*
#5 (#1 OR #2 OR #3 OR #4)
#6 MeSH descriptor Respiration, Artificial, this term only
#7 artificial near ventil*
#8 Ventilat* near mechanical

#9 MeSH descriptor Intubation, Intratracheal, this term only
#10 MeSH descriptor Respiratory Insufficiency explode all trees
#11 (respiratory failure) or (respiratory near failure)
#12 MeSH descriptor Suction explode all trees
#13 (#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12)
#14 (#5 AND #13) (limit record entry: 2010-2014; in trials only)

EMBASE search strategy (Emtree)

#1 'music therapy'/exp
#2 music* OR rhythm* OR melod*
#3 singing OR song* OR listening OR improvis*
#4 #1 OR #2 OR #3
#5 'artificial ventilation'/de
#6 artificial NEAR/10 ventilat*
#7 ventilat* NEAR/10 mechanical
#8 'endotracheal intubation'/exp
#9 'respiratory failure'/exp
#10 respiratory NEAR/10 failure
#11 'airway suction'
#12 #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
#13 'randomized controlled trial'/exp
#14 'controlled clinical trial'/exp
#15 randomized:ab
#16 randomly:ab
#17 trial:ab
#18 groups:ab
#19 #13 OR #14 OR #15 OR #16 OR #17 OR #18
#20 'human'/exp
#21 #19 AND #20
#22 #4 AND #12 AND #21
#23 #22 AND (2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py)

CINAHL search strategy (EBSCOhost)

S1 TX compos* or TX singing or TX sing or TX song* or TX music* or TX rhythm* or TX melod* or MH music or MH music therapy
S2 (MH "Intubation, Intratracheal") or (MH "Extubation") or (MH "Suction") or (MH "Suctioning, Endotracheal") or (MH "Airway Suctioning") or TX ventilator N5 weaning or TX respiratory N5 failure or (respiratory failure) or (MH "Respiratory Failure") or (MH "Ventilator Weaning") or TX Ventilat* N5 mechanical or TX artificial N5 ventil* or respiratory insufficiency or (artificial respiration) or (MH "Ventilation, Mechanical+") or (MH "Ventilators, Mechanical")
S3 (S1 and S2) not animal* (limit 20100101-20141231)

LILACS search strategy (Virtual Health Library)

(music$) and ((mechanical and ventilation) or (intratracheal and intubation) or (respiratory and failure) or "RESPIRATORY FAILURE" or (artificial and respiration) or (suction) or "SUCTION")
(this database does not have the capacity to apply date limits. Results outputs were reviewed from 2008 onward)

ISI Web of Science search strategy

#1 TS=(Respiration artificial) or TS=(artificial SAME ventil*) or TS=(Ventilat* SAME mechanical) or TS=(Intubation SAME intra-tracheal) or TS=(respiratory insufficiency) or TS=(respiratory SAME failure)

#2 TS=music* or TS=(music therapy) or TS=(singing or song or song* or compos* or improvis* or rhythm* or melod*) or TS=(suction)
#3 TS=(control$ or prospectiv$ or volunteer$) or TS=(prospective studies) or TS=(follow up studies) or TS=(evaluation studies) or TS=(comparative study) or TS=random$ or TS=placebo$ or TS=(Clinical trial$) or TS=(single-blind method$) or TS=(double blind method$) or TS=(randomized controlled trial$) or TS=(controlled clinical trial$) or TS=(random allocation)
#4 #1 and #2 and #3
#5 Timespan = 2010-2014

CAIRSS for Music search strategy (Webvoyage)

("mechanical ventilation")[in Keyword Anywhere] OR ("artificial ventilation")[in Keyword Anywhere] OR
("artificial respiration")[in Keyword Anywhere]
(intubation)[in Keyword Anywhere] OR ("suction")[in Keyword Anywhere]
("respiratory failure" [in Keyword Anywhere] OR ("respiratory insufficiency")[in Keyword Anywhere]

Proquest Digital Dissertations search strategy (Proquest)

ab(mechanical* ventilat*) AND ab(Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)
ab(artificial* respirat*) AND ab(Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)
ab(articicial* ventilat*) AND ab(Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)
ab(intubation or suction) AND ab(Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)
ab(respirat* insufficien*) AND ab(Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)
ab(respirat* failure) AND ab(Singing or sing or song* or compos* or improvis* or music* or rhythm* or melod*)

Clinical trials.gov search strategy

(music or "music therapy") (limits by date first received: 01/01/2010 - 03/24/2014)

Current Controlled Trials search strategy

music
music therapy

National Research Registry search strategy

music

NIH CRISP search strategy

music

WHAT'S NEW

Last assessed as up-to-date: 24 March 2014.

Date	Event	Description
9 December 2014	New search has been performed	In the previous version (Bradt 2010) the databases were searched until 2010. In this updated version we reran the searches until 24 March 2014. We also extended our handsearching to include two additional journals namely the Japanese Music Therapy Association Journal and Music and Medicine. In this updated review, we have revised the risk of bias tables of all studies according to the new Cochrane Collaboration's risk of bias tool
9 December 2014	New citation required and conclusions have changed	This review is an update of the previous Cochrane review (Bradt 2010) that included eight studies. One of the previous authors, Dr Denise Grocke, decided not to participate in the update of this review This updated review includes six new trials. Our conclusions about the impact of music interventions on state anxiety in mechanically ventilated patients remains similar to those in Bradt 2010. However, the addition of trials examining this outcome resulted in more precise estimates. The conclusions for the effect of music interventions on physiological responses has changed for several of the outcomes (for example, systolic blood pressure). For other outcomes, a more precise estimate was reached because of the added studies Whereas the previous review did not identify studies that included sedative and analgesic drug intake and mortality as outcomes, we were able to include several studies that addressed these outcomes in this update

HISTORY

Protocol first published: Issue 1, 2008

Review first published: Issue 12, 2010

Date	Event	Description
13 June 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Joke Bradt (JB), Cheryl Dileo (CD) (and in original review Denise Grocke (DG) (Bradt 2010))

Conceiving the review: CD

Co-ordinating the review: JB

Undertaking manual searches: JB, DG, and graduate assistants

Screening search results: CD,JB, and graduate assistants

Organizing retrieval of papers: JB

Screening retrieved papers against inclusion criteria: JB

Appraising quality of papers: CD and JB

Abstracting data from papers: JB and research assistant

Writing to authors of papers for additional information: JB

Providing additional data about papers: JB

Obtaining and screening data on unpublished studies:CD

Data management for the review: JB

Entering data into Review Manager (RevMan 5.2): JB and research assistant

RevMan statistical data: JB

Other statistical analysis not using RevMan: JB

Double entry of data: (data entered by person one JB; data entered by person two: research assistant)

Interpretation of data: CD, JB, DG for original review; JB and CD for update

Statistical inferences: JB

Writing the review: CD, JB, DG for original review; JB and CD for update

Securing funding for the review: CD for original review; no funding for update

Guarantor for the review (one author): JB

Person responsible for reading and checking review before submission: JB

DECLARATIONS OF INTEREST

Joke Bradt and Cheryl Dileo are music therapists

The original review (Bradt 2010) was partly supported by a grant of the State of Pennsylvania Formula Fund. No funding was received for the update of the review.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- State of Pennsylvania Formula Fund, USA.

Financial support for the original review (Bradt 2010)

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Bradt 2010

In the protocol (Bradt 2008), we stated that we would exclude studies that used systematic methods of randomization. However, because only a small number of studies met all inclusion criteria, we decided to include studies that used systematic randomization (for example, alternate assignment). We analysed the impact of these studies by means of sensitivity analysis.

The Specialist Music Therapy Research database is no longer a functional database. However, archives of research reports, dissertations, and conference proceedings are still available for handsearching. The authors handsearched these files.

INDEX TERMS

Medical Subject Headings (MeSH)

Anxiety [*therapy]; Blood Pressure [physiology]; Heart Rate [physiology]; Music [*psychology]; Music Therapy [*methods]; Randomized Controlled Trials as Topic; Respiration, Artificial [adverse effects; *psychology]; Respiratory Rate [physiology]; Standard of Care

MeSH check words

Humans