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Use of music to enhance sleep and psychological outcomes in critically ill patients: a protocol for systematic review and meta-analysis

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LX was responsible for drafting the article or revising it critically for important intellectual content. JH and CL conducted final approval of the version to be submitted. DH, SQ and QY were responsible for the conception and design of the study, XL supervised the work. All authors approved the final version of the article.

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Abstract

Introduction Music as a non-pharmacological intervention, is widely used in various populations with positive results, yet the evidence for music on sleep and psychological outcomes in critically ill patients is less clear. It is essential to better understand the impact of music listening for critically ill patients to optimise care and minimise risk of harm. We will assess whether music listening improves sleep and psychological outcomes in critically ill patients.

Methods and analysis We will systematically search scientific databases: PubMed, Embase, CINAHL, PsycINFO, Web of Science, Scopus, ProQuest, the Cochrane Central Register of Controlled Trials, China Biological Medicine Database, China National Knowledge Infrastructure Library, Wan fang databases, VIP Database for Chinese Technical Periodicals, and the Chinese Clinical Trial Registry. All databases will be searched for articles published from their start date to January 2020. Music therapy journals and reference lists in some articles will be hand-searched. Gray literature will also be searched. We will include randomized and quasi-randomized controlled trials of music listening to improve sleep and psychological outcomes in critically ill patients. The primary outcomes will be sleep-related outcomes, the secondary outcomes will be anxiety score, depression score and physiological outcomes. Two reviewers will independently verify study eligibility and methodological quality; disagreements will be resolved by a third reviewer or discussion. The risk of bias will be independently determined using the Cochrane Risk of Bias Tool. Data will be extracted from eligible studies by two researchers. RevMan (version 5.3) will be used for meta-analysis. Additionally, the CONSORT checklist will be used to examine the quality of the papers.

Ethics and Dissemination This work will review existing trial data and will not introduce new patient data or interventions, ethics committee approval is not required. We will disseminate this protocol in a related peer-reviewed journal.

PROSPERO Registration Number CRD42019147202

Strengths and limitations of this study

This research identify the effectiveness of music listening for sleep, anxiety, and depression in critically ill patients. A comprehensive search strategy will be used in a large number of databases to maximise the identification of all eligible studies.

Primary screening of the studies, data collection and validation, methodological quality assessment, data extraction and analysis will be performed independently by two researchers with extensive experience in systematic review methodology, to minimise the probability of personal biases.

In this study, the investigators will confine the analysis to articles published in Chinese or English, French, German, Spanish, etc will not be searched or included. This limitation may cause language bias.

INTRODUCTION

Rationale

Sleep disturbance is a frequent problem among patients in intensive care units (ICUs)[1]. Sleep quality and quantity[2] are negatively affected by the ICU environment (e.g., noise, lights), patient-care activities, symptoms of the patient's underlying illness, and by mechanical ventilation[3 4]. It is characterized by prolonged sleep onset latency, short sleep duration, frequent awakenings, non-restorative sleep, and decreased sleep efficiency (percentage of time in bed spent asleep). Sleep disturbance has been associated with numerous adverse consequences in critically ill patients, including impairments in immune function, memory, wound healing, and inspiratory muscle endurance; higher rates of delirium; and increased overall morbidity and mortality[5].

An increase in psychological problems, such as anxiety and depression, has also been found in critically ill patients[6 7]. One study estimated that 70%–80% of critically ill patients suffer anxiety related to fear, sleeplessness, pain, discomfort, thirst, and disease-related symptoms; patients on assisted ventilation were especially prone to anxiety because of their need for frequent suctioning, inability to breath independently or talk, and general discomfort. It has also been found that one-half of patients experienced a high level of depression during the ICU stay[8]. In turn, unmanaged anxiety and depression have been associated with harmful effects on disease recovery and overall well-being: prolonged weaning from ventilation and recovery time[9], increased work of breathing, fatigue[10], and acute elevations in blood pressure[11], increase the depression incidence in ICU survivors[12]. Wewalka found that pre-existing depressive mood at the time of ICU admission was an independent risk factor for 28-day mortality in medical ICU patients[13].

Sufficient evidence showed that sleep disturbance, anxiety and depression were detrimental to their disease recovery and psychological well-being. Research has also reported the interplay of sleep disturbance, anxiety, and depression[14]. Anxiety and depression are both risk factors for sleep disturbance, and disturbed sleep pattern in turn increases emotional distress, leading to higher levels of anxiety and depression[15 16]. Therefore, nurses as key staffs in the ICU, need to provide effective interventions to address all of these.

Pharmacological and non-pharmacological interventions are proposed to manage sleep and psychological distress in the ICU. Pharmacological therapy is generally the first line of treatment[17 18]. However, pharmacological therapy itself has been associated with numerous adverse effects and complications, including memory loss, prolongation of mechanical ventilation, altered sleep stages, longer length of hospitalization, tolerance, bradycardia, hypotension, residual daytime effects, dysmotility, weakness, and delirium[19 20]. Additionally, the medications used are expensive. To avoid

this, a number of researchers have developed alternative, non-pharmacological therapies to improve sleep, anxiety, and depression in ICU patients, with positive results[21-23].

The use of music is one such non-pharmacological intervention adopted by nurses. As far back as the early 1800s, Florence Nightingale[24] described the importance of music and its healing effect on patients. Music therapy and music listening are common form of music intervention, it is very important to distinguish them. According to some studies, music therapy is normally implemented by trained music therapists. Music listening is defined as listening to recorded music via any form of music device, or live music, without interaction with a music therapist, as a form of music intervention, it is provided by medical or healthcare professionals or is self-administered by the patient[25 26]. More recently, music listening has been widely used in various diseases, such as Parkinson disease[27], Alzheimer disease[28], and cancer[29], to assuage emotional, physiological, and psychological symptoms. A growing number of studies, in adults of all ages, have demonstrated the positive effects of music listening on anxiety, depression, stress, and pain[30-32], in various medical and surgical conditions. Repeated studies have specifically reported music listening improved sleep in critically ill patients[23 33 34]. Furthermore, music listening is inexpensive, relatively easy to carry out, and safe compared with pharmacological intervention[35], benefits that are favourably received by patients. Thus, music listening is a potentially viable alternative treatment option.

Clinical trials have provided support for the effectiveness of music therapy in the healthcare setting, psychophysiological theory[36] also provides clues to its mechanism of action. Earlier authors described that sleep improvement is mediated by the relaxing, distracting effect of 'soothing' music[37]. Music with a slow tempo of 60–80 beats per minute mirrors the heart rate and reduces neuroendocrine and sympathetic nervous system activity, resulting in relaxation. Further, the peaceful atmosphere created by soothing music in the ICU setting is a mood enhancer, reducing anxiety and depression, and lowering treatment-related stress. Elsewhere, other authors described the effect of music in modulating mood and emotions at the cortical level, through stimulation of self-image and intellect [38]. Clinical trials have also shown that listening to music reduced anxiety and stress responses—which can lead to greater relaxation and improvement of sleep[39 40].

Research on the impact of music listening for ICU patients has evolved during the past 20 years, several researchers studied the effects of music listening on sleep and psychological outcomes in critically ill patients. For example, recent studies reporting that music listening may improve stress, anxiety[7 41], depression[42] and sleep[43 44] in ICU patients. The intervention involves different types of music to improve sleep and psychological symptoms, such as low volume, nature sounds, soothing music, Mozart piano, etc. Music listening can be provided by specific tools (e.g. Mp3 or earphones or loudspeaker). The choice of music may be determined by the researcher or by participants

themselves. The duration, frequency, and timing of music exposure has also varied among studies. Although clinical trials have been performed to investigate the effects of music listening on sleep and psychological outcomes, their safety and efficacy for critically ill patients have not been established. Most of these studies have suffered from small sample size[34 45], making it nearly impossible to achieve statistically significant results. The impact of the music listening may differ due to the different design of the intervention (study design, methods of intervention, and types of music). One systematic review have assessed the efficacy of music interventions for reducing anxiety in mechanically ventilated patients[26], the author only included mechanically ventilated patients. A recent systematic review also evaluated the effectiveness of music therapy to reduce stress and anxiety in critically ill patients[46]. In 2015, another review reported that music therapy appeared to be safe to improve sleep but did not do a meta-analysis, and further randomized controlled trials were required to assess efficacy[47]. The 2018 Pain, Agitation/ sedation, Delirium, Immobility (rehabilitation/mobilization), and Sleep (disruption) (PADIS) guideline also suggest no high quality evidence to prove that music could improve sleep in critically ill adults[1].

Until now, despite the large number of relevant studies, music listening has not been implemented as a therapeutic intervention in everyday critical care because information about effectiveness has not been synthesised and disseminated universally. So, we assess effectiveness of music listening in improvement of sleep, anxiety and depression in critically ill patients, and investigate relevant subgroups (timing of intervention, type of intervention, severity of disease, mechanical ventilation status, and study site).

OBJECTIVES

This systematic review and meta-analysis aim to integrate the scientific research on the use of music listening to promote sleep, anxiety, and depression for critically ill patients in ICU. We attempt to answer the following research questions:

1.What are the effects of music listening on sleep quality and quantity in critically ill patients?

2.What are the effects of music listening on anxiety, depression and physiological outcomes in critically ill patients?

METHODS AND ANALYSIS

This is a quantitative systematic review protocol. We will follow the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines to complete and report the study protocol[48]. This systematic review protocol has been registered in PROSPERO (PROSPERO Registration Number CRD 42019147202)

Inclusion/Exclusion criteria

Types of participants

Studies will be selected for inclusion if their subjects meet the criteria:

- adult patient in the ICU,
- non-sedated,
- ventilated or non-ventilated,
- Glasgow Coma Scale score ≥14,
- admittance to the ICU ≥24 hours.

We will exclude studies whose subjects were:

- diagnosed with / had overt signs or symptoms of obstructive sleep apnoea or hearing damage,
- terminally ill or in palliative care,
- diagnosed with dementia or neurologic disease.

Types of intervention and comparison

We will include any study of improved sleep or psychological outcomes in which music listening and standard care with standard care alone, or standard care with other interventions in critically ill patients.

Types of outcome measures

At least one of the following outcomes must have been reported in the study:

Primary outcomes

- Sleep outcomes
  1. Sleep quality
  2. Sleep onset latency
  3. Total sleep time
  4. Number of awakenings
  5. Sleep efficiency (percent of time in bed spent asleep)

Sleep outcomes are measured using a variety of methods. Subjective perception of sleep is measured through validated self-report tools, including the Richards–Campbell Sleep Questionnaire (RCSQ)[49], Pittsburgh Sleep Quality Index (PSQI)[50], and the Verran and Synder-Halpern (VSH) Sleep Scale[51]; objective measurement of sleep is done with polysomnography, actigraphy, bispectral index (BIS) monitoring, or electroencephalography (EEG).

Secondary outcomes

- Psychological outcomes
  1. Anxiety

2. Depression

We will include trials that measured psychological outcomes using standardized questionnaires with established reliability and validity, including Hospital-based Anxiety and Depression Scales[52], the Visual Analogue Scale for Anxiety (VAS-A)[53], the Spielberger State-Trait anxiety Inventory[54], and the Beck Anxiety Inventory[55].

- Physiological outcomes (heart rate, blood pressure, respiratory rate)

Types of study designs

We will include any interventional study, including randomized and quasi-randomized controlled trials.

Data source and search strategy

To identify eligible studies, we will search electronic databases, including: PubMed, Embase, CINAHL, PsycINFO, Web of Science, Scopus, ProQuest, the Cochrane Central Register of Controlled Trials, China Biological Medicine Database, China National Knowledge Infrastructure Library, Wang fang databases, VIP Database for Chinese Technical Periodicals, the Chinese Clinical Trial Registry. The databases will be searched from their start date to October 2019. Additionally, we will hand-search music therapy journals and the reference lists in some articles, as well as gray literature.

A health sciences librarian will design the search. Table 1 shows the search strategy, employing both keywords and Medical Subject Heading (MeSH) terms, that will be used to search PUBMED; this will be adapted for the other databases.

Selection of studies

All articles retrieved through the search of the selected databases will be imported to Endnote, from which duplicate references will be removed. Two members of the research team (SQ and QY) will independently review the title/abstract of each article to verify each study meets the inclusion criteria; if a title or abstract is unclear, the two researchers will review the full article. Disagreements will be resolved by a third researcher (LX) or through discussion until consensus is reached. The reason for all exclusions will be recorded.

Data collection and validation

Two researchers (JH and CL) will independently extract data from the included studies, using the Cochrane Collaboration Data Collection Form[56]. In the event of questions or missing data in the original text, the researchers will contact the author to obtain the relevant data. The results of data extraction will be compared to exclude any differences, and any disagreement will be resolved by a third researcher (LX) or through discussion and consensus.

From all included studies, we will collect the following data:

1. Research and publication information, including the title, journal (volume, page number) or if unpublished, the author, year of publication, country, and setting, the language of publication, and funding sources;

2. Study design, including the type of design, inclusion criteria, exclusion criteria, randomization method (including concealment and blinding), and losses to follow up;

3. Characteristics of the subjects, including total sample size, number of participants in the intervention and control groups, gender, age, diagnosis, disease severity (Acute Physiology and Chronic Health Evaluation [APACHE] II scores), comorbidities, and mechanical ventilation status;

4. Intervention details, including type of music, control of music selection (by participant or researcher), the frequency, duration, and timing of music listening, and the format/devices used (e.g., headphone, loudspeaker); and

5. Outcomes, including the methods of assessment of sleep, anxiety, and depression, pre- and post-test means or change scores, and standard deviations.

Methodological quality assessment

The risk of bias and quality of the included studies will be evaluated using the Cochrane Collaboration's Risk for Bias tool[57], which evaluates seven sources of study bias: 1) random sequence generation, 2) allocation concealment, 3) performance bias, 4) detection bias, 5) incomplete outcome data, 6) selective reporting, and 7) other bias. Two researchers (LX and XL) will independently grade each element as 'low risk', 'high risk', or 'unclear risk'[58]. Inconsistencies will be resolved through discussion and consensus, or by a third researcher (DH). For quality assessment of quasi-randomized controlled trials, an appropriate assessment will be completed.

Data synthesis and analysis

A meta-analysis will be conducted once there are a sufficient number of studies showing homogeneity. The statistical analysis will be performed using RevMan 5.3.5 software. Continuous data will be expressed with the odds ratio (OR) and its 95% confidence interval (CI). The level of heterogeneity of the included studies will be determined with the I2 statistic and P value[59]. If P>0.1 and I2<50%, suggesting no statistical heterogeneity, a meta-analysis will be performed using a fixed-effects model; if I2>50%, a random-effects model will be used to analyse the clinical heterogeneity. Subgroup analysis will be performed by: timing of intervention, type of intervention, severity of disease (APACHE II score <25, 25–35, >35), mechanical ventilation status (ventilated patients versus non-ventilated patients), and study site (surgical ICU patients versus medical ICU patients). Sensitivity analysis will be used to determine the stability of the results, and Egger's regression test and funnel plots will be used to assess potential publication bias. If data pooling is not possible,

quantitative data will be presented in a narrative review of the study primary and secondary outcomes, using thematic summaries and tables.

Validity and reliability /Rigour

The study protocol will use systematic review and meta-analytic methods, following the Cochrane Collaboration recommendations for performing a systematic review. The results will be reported according to the PRISMA-P guidelines[60]. Additionally, the CONSORT checklist will be used to examine the quality of the papers.

DISCUSSION

This paper presents the protocol for a systematic review of the literature examining the effects of music listening on sleep and psychological outcomes in critically ill patients. The study was undertaken to answer questions about the effectiveness of music listening in this population and to our knowledge, is the first to analyse the body of Chinese and English research on this topic. Properly powered, intervention studies provide strong evidence, so this meta-analysis of the existing evidence will permit conclusions about the efficacy of music listening on sleep, anxiety, and depression in critically ill patients. Results from this project will provide recommendations for the use of music listening in this population and will support nurses and other health practitioners in their promotion of mental health. Additionally, by identifying existing lacunae in the literature, our results will prompt further research.

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Table 1 Search strategy for PubMed

Filter: Humans
1 music [Mesh] OR 'music therapy' [Mesh] OR music* OR listen*
2 sleep [Mesh] OR sleep Disorders, Circadian Rhythm [Mesh] OR sleep* OR insomnia* OR wakeful* OR sleepless*
3 anxiety [Mesh] OR fear [Mesh] OR stress OR psychological OR depression [Mesh] OR depress* OR mood disorders [Mesh]
4 2 OR 3
5 critical illness [Mesh]) OR critical care [Mesh] OR 'intensive care units' [Mesh] OR ventilators, mechanical [Mesh] OR respiration, artificial [Mesh] OR intensive care OR ICU
6 **1 AND 4 AND 5**
7 infant* OR neonat* OR infant, premature [Mesh] OR infant, newborn [Mesh] OR Intensive Care Units, pediatric [Mesh]
8 6 NOT 7

PRISMA 2009 Checklist

Section / topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	8
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

Use of music to enhance sleep and psychological outcomes in critically ill patients: a protocol for systematic review and meta-analysis

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Use of music to enhance sleep and psychological outcomes in critically ill patients: a protocol for systematic review and meta-analysis

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Contributors

Lixia Chen was responsible for drafting the article or revising it critically for important intellectual content. Jianhua Li and Li Cui conducted final approval of the version to be submitted. Xiaoli Liu, Siqi Qu, and Cuihua Han were responsible for the conception and design of the study, Daihong Ji supervised the work. All authors approved the final version of the article.

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Abstract

Introduction Music listening as a non-pharmacological intervention, is widely used in various populations with positive results, yet the evidence for music listening on sleep and psychological outcomes in critically ill patients is less clear. It is essential to better understand the impact of music listening for critically ill patients to optimise care and minimise risk of harm. We will assess whether music listening improves sleep and psychological outcomes in critically ill patients.

Methods and analysis We will systematically search scientific databases: PubMed, Embase, CINAHL, PsycINFO, Web of Science, Scopus, ProQuest, the Cochrane Central Register of Controlled Trials, China Biological Medicine Database, China National Knowledge Infrastructure Library, Wan fang databases, VIP Database for Chinese Technical Periodicals, and the Chinese Clinical Trial Registry. All databases will be searched for articles published from inception to 10 June 2020. Music therapy journals and reference lists in some articles will be hand-searched. Gray literature will also be searched. We will include randomized and quasi-randomized controlled trials of music listening to improve sleep and psychological outcomes in critically ill patients. The primary outcomes will be sleep-related outcomes, the secondary outcomes will be anxiety score, depression score and physiological outcomes. Two reviewers will independently verify study eligibility and methodological quality; disagreements will be resolved by a third reviewer or discussion. The risk of bias will be independently determined using the Cochrane Risk of Bias Tool. Data will be extracted from eligible studies by two researchers. RevMan (version 5.3) will be used for meta-analysis. Additionally, the CONSORT checklist will be used to examine the quality of the papers.

Ethics and Dissemination This work will review existing trial data and will not introduce new patient data or interventions, ethics committee approval is not required. We will disseminate this protocol in a related peer-reviewed journal.

PROSPERO Registration Number CRD42019147202

Strengths and limitations of this study

- We plan to employ robust international gold-standard methodology and comprehensive search strategy to reduce bias.
- We will assess the quality of the articles included using a validated tool.

- Subgroup analysis will be performed when possible to elaborate intervention or subject characteristics correlated with increased effectiveness.
- If there is high heterogeneity across studies, which may increase the difficulties to interpret a meta- analysis.
- Limited in that the systematic review protocol will only include articles in English and Chinese.

INTRODUCTION

Rationale

Sleep disturbance is a frequent problem among patients in intensive care units (ICUs)[1 2]. Sleep quality and quantity[3] are negatively affected by the ICU environment (e.g., noise, lights), patient-care activities, symptoms of the patient's underlying illness, and by mechanical ventilation[4 5]. It is characterized by prolonged sleep onset latency, short sleep duration, frequent awakenings, non-restorative sleep, and decreased sleep efficiency (percentage of time in bed spent asleep). Sleep disturbance has been associated with numerous adverse consequences in critically ill patients, including impairments in immune function, memory, wound healing, and inspiratory muscle endurance; higher rates of delirium; and increased overall morbidity and mortality[6].

An increase in psychological problems, such as anxiety and depression, has also been found in critically ill patients[7 8]. One study[9] estimated that 70%–80% of critically ill patients suffer anxiety related to fear, sleeplessness, pain, discomfort, thirst, and disease-related symptoms; patients on assisted ventilation were especially prone to anxiety because of their need for frequent suctioning, inability to breath independently or talk, and general discomfort. It has also been found that one-half of patients experienced a high level of depression during the ICU stay[9]. In turn, unmanaged anxiety and depression have been associated with harmful effects on disease recovery and overall well-being: prolonged weaning from ventilation and recovery time[10], increased work of breathing, fatigue[11], and acute elevations in blood pressure[12], increase the depression incidence in ICU survivors[13]. Wewalka found that pre-existing depressive mood at the time of ICU admission was an independent risk factor for 28-day mortality in medical ICU patients[14].

Sufficient evidence showed that sleep disturbance, anxiety and depression were detrimental to their disease recovery and psychological well-being. Research has also reported the interplay of sleep disturbance, anxiety, and depression[15]. Anxiety and depression are both risk factors for sleep disturbance, and disturbed sleep pattern in turn increases emotional distress, leading to higher levels of anxiety and depression[16 17]. Therefore, nurses as key staffs in the ICU, need to provide effective interventions to address all of these.

Pharmacological and non-pharmacological interventions are proposed to manage sleep and psychological distress in the ICU. Pharmacological therapy is generally the first line of treatment[18 19]. However, pharmacological therapy itself has been associated with numerous adverse effects and

complications, including memory loss, prolongation of mechanical ventilation, altered sleep stages, longer length of hospitalization, tolerance, bradycardia, hypotension, residual daytime effects, dysmotility, weakness, and delirium[20 21]. Additionally, the medications used are expensive. To avoid this, a number of researchers have developed alternative, non-pharmacological therapies to improve sleep, anxiety, and depression in ICU patients, with positive results[22-24]. In recent years, the results of music intervention studies had led scientists to pay close attention to the relationship between music and sleep in various types of patients. This has resulted in an increase in the use of music therapy and music listening (sometimes called music medicine[25]).

Music is a non-pharmacological intervention that can be adopted by nurses. It is relatively easy to implement, cost effective, safe and has no negative impacts[26]. As far back as the early 1800s, Florence Nightingale[27] described the importance of music and its healing effect on patients. Music therapy and music listening are common forms of music interventions that are similar but have distinct features. Music therapy is defined as the clinical and evidence-based use of music interventions to realize individualized clinical goals within a therapeutic relationship. It is conducted by a licensed music therapist, and centres on the dynamic musical interaction between the music therapist and the patient, verbal processing of the music experience, and implementation and alteration of recorded music (tempo, volume, intensity) according to the patient's psychological and physiological state to induce a relaxation response, etc[28]. The use of environmental music therapy, which is a method of live music therapy, has been increasing in recent years[29 30]. Music listening is defined as passive listening to recorded music via any form of music playback device (e.g. listening to a MP3 through earphones or a loudspeaker) or listening to live music, without interacting with a music therapist or theoretical framework. It can be provided by medical or healthcare professionals or self-administered by a patient, and patients may or may not be involved in selecting the music[31 32]. It is necessary to distinguish the two interventions in clinical practice[33] due to the varying levels of training in the fundamentals of music and its therapeutic applications. For instance, music therapists receive specialized training in the aforementioned areas[25]. Music listening can also facilitate music therapy, and compared with music therapy, music listening is easier to implement in the ICU, is more convenient and is low-cost. More recently, music listening has been widely used in various diseases, such as Parkinson disease[34], Alzheimer disease[35], and cancer[36], to assuage emotional, physiological, and psychological symptoms. A growing number of studies, in adults of all ages, have

demonstrated the positive effects of music listening on anxiety, depression, stress, and pain[37 38], in various medical and surgical conditions. Repeated studies have specifically reported music listening improved sleep in critically ill patients[24 39 40]. Furthermore, music listening is inexpensive, relatively easy to carry out, and safe compared with pharmacological intervention[26], benefits that are favourably received by patients. Thus, music listening is a potentially viable alternative treatment option.

Clinical trials have provided support for the effectiveness of music intervention in the healthcare setting, psychophysiological theory[41] also provides clues to its mechanism of action. Music is made up of many key elements, including rhythm, pitch, harmony, and melody. These music elements play a comprehensive role in the degree to which music can promote sleep in patients[42]. Earlier authors described that sleep improvement is mediated by the relaxing, distracting effect of 'soothing' music[43]. Music with a slow tempo of 60–80 beats per minute mirrors the heart rate and reduces neuroendocrine and sympathetic nervous system activity, resulting in relaxation. Further, the peaceful atmosphere created by soothing music in the ICU setting is a mood enhancer, reducing anxiety and depression, and lowering treatment-related stress. Elsewhere, other authors described the effect of music in modulating mood and emotions at the cortical level, through stimulation of self-image and intellect[44]. Clinical trials have also shown that listening to music reduced anxiety and stress responses—which can lead to greater relaxation and improvement of sleep[45 46].

Research on the impact of music listening for ICU patients has evolved during the past 20 years, several researchers studied the effects of music listening on sleep and psychological outcomes in critically ill patients. For example, recent studies reporting that music listening may improve stress, anxiety[8 47], depression[48] and sleep[49 50] in ICU patients. The intervention involves different types of music to improve sleep and psychological symptoms, such as low volume, nature sounds, soothing music, Mozart piano, etc. Music listening can be provided by specific tools (e.g. Mp3 or earphones or loudspeaker). The choice of music may be determined by the researcher or by participants themselves. The duration, frequency, and timing of music exposure has also varied among studies. Although clinical trials have been performed to investigate the effects of music listening on sleep and psychological outcomes, their safety and efficacy for critically ill patients have not been established. Most of these studies have suffered from small sample size[40 51], making it nearly impossible to

achieve statistically significant results. The impact of the music listening may differ due to the different design of the intervention (study design, methods of intervention, and types of music). One systematic review have assessed the efficacy of music interventions for reducing anxiety in mechanically ventilated patients[32], the author only included mechanically ventilated patients. A recent systematic review also evaluated the effectiveness of music therapy to reduce stress and anxiety in critically ill patients[52]. In 2015, another review reported that music therapy appeared to be safe to improve sleep but did not do a meta-analysis, and further randomized controlled trials were required to assess efficacy[53]. The 2018 Pain, Agitation/ sedation, Delirium, Immobility (rehabilitation/mobilization), and Sleep (disruption) (PADIS) guideline also suggest no high quality evidence to prove that music could improve sleep in critically ill adults[1].

Until now, despite the large number of relevant studies, music listening has not been implemented as a therapeutic intervention in everyday critical care because information about effectiveness has not been synthesised and disseminated universally. So, we assess effectiveness of music listening in improvement of sleep, anxiety and depression in critically ill patients, and investigate relevant subgroups (timing of intervention, type of intervention, severity of disease, mechanical ventilation status, and study site).

OBJECTIVES

This systematic review and meta-analysis aim to integrate the scientific research on the use of music listening to promote sleep, anxiety, and depression for critically ill patients in ICU. We attempt to answer the following research questions:

1.What are the effects of music listening on sleep quality and quantity in critically ill patients?

2.What are the effects of music listening on anxiety, depression and physiological outcomes in critically ill patients?

METHODS AND ANALYSIS

This is a quantitative systematic review protocol. We will follow the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines to complete and report the study protocol[54]. This systematic review protocol has been registered in PROSPERO (PROSPERO Registration Number CRD 42019147202)

Patient and public involvement

No patient and public involved in this study.

Inclusion/Exclusion criteria

Types of participants

Studies will be selected for inclusion if their subjects meet the criteria:

- adult patient in the ICU (age>18 years old),
- being conscious and clear (Glasgow Coma Scale score ≥14),
- ventilated or non-ventilated,
- admittance to the ICU ≥24 hours.

We will exclude studies whose subjects had:

- hearing damage,
- been diagnosed with / had overt signs or symptoms of obstructive sleep apnea,
- been diagnosed with dementia or neurologic disease,
- severe signs or symptoms of psychological illness, such as hallucinations, delusions, and behavioral disorders, etc.

Types of intervention and comparison

We will include any study in which sleep or psychological variables were considered as outcomes of music listening combined with standard care vs. standard care alone or standard care with other interventions in critically ill patients.

Types of outcome measures

At least one of the following outcomes must have been reported in the study:

Primary outcomes

- Sleep outcomes
  1. Sleep quality
  2. Sleep onset latency
  3. Total sleep time
  4. Number of awakenings
  5. Sleep efficiency (percent of time in bed spent asleep)

Sleep outcomes are measured using a variety of methods. Subjective perception of sleep is measured through validated self-report tools, including the Richards–Campbell Sleep Questionnaire (RCSQ)[55],

Pittsburgh Sleep Quality Index (PSQI)[56], and the Verran and Synder-Halpern (VSH) Sleep Scale[57]; objective measurement of sleep is done with polysomnography, actigraphy, bispectral index (BIS) monitoring, or electroencephalography (EEG).

Secondary outcomes

- Psychological outcomes
  1. Anxiety
  2. Depression

We will include trials that measured psychological outcomes using standardized questionnaires with established reliability and validity, including Hospital-based Anxiety and Depression Scales[58], the Visual Analogue Scale for Anxiety (VAS-A)[59], the Spielberger State-Trait anxiety Inventory[60], and the Beck Anxiety Inventory[61].

- Physiological outcomes (heart rate, blood pressure, respiratory rate)

Types of study designs

We will include any interventional study, including randomized and quasi-randomized controlled trials.

Data source and search strategy

To identify eligible studies, we will search electronic databases, including: PubMed, Embase, CINAHL, PsycINFO, Web of Science, Scopus, ProQuest, the Cochrane Central Register of Controlled Trials, China Biological Medicine Database, China National Knowledge Infrastructure Library, Wang fang databases, VIP Database for Chinese Technical Periodicals, the Chinese Clinical Trial Registry. The databases will be searched from their start date to October 2019. Additionally, we will hand-search music therapy journals and the reference lists in some articles, as well as gray literature.

A health sciences librarian will design the search. Table 1 shows the search strategy, employing both keywords and Medical Subject Heading (MeSH) terms, that will be used to search PUBMED; this will be adapted for the other databases.

Table 1 Search strategy for PubMed

Filter: Humans
1 music [Mesh] OR 'music therapy' [Mesh] OR music medicine OR music* OR listen*
2 sleep [Mesh] OR sleep Disorders, Circadian Rhythm [Mesh] OR sleep* OR insomnia* OR wakeful* OR sleepless*
3 anxiety [Mesh] OR fear [Mesh] OR stress OR psychological OR depression [Mesh] OR depress* OR mood disorders [Mesh]
4 2 OR 3
5 critical illness [Mesh]) OR critical care [Mesh] OR 'intensive care units' [Mesh] OR ventilators, mechanical [Mesh] OR respiration, artificial [Mesh] OR intensive care OR ICU
6 **1 AND 4 AND 5**
7 infant* OR neonat* OR infant, premature [Mesh] OR infant, newborn [Mesh] OR Intensive Care Units, pediatric [Mesh]
8 6 NOT 7

Selection of studies

All articles retrieved through the search of the selected databases will be imported to Endnote, from which duplicate references will be removed. Two members of the research team (SQ and CH) will independently review the title/abstract of each article to verify each study meets the inclusion criteria; if a title or abstract is unclear, the two researchers will review the full article. Disagreements will be resolved by a third researcher (LX) or through discussion until consensus is reached. The reason for all exclusions will be recorded.

Data collection and validation

Two researchers (JH and CL) will independently extract data from the included studies, using the Cochrane Collaboration Data Collection Form[62]. In the event of questions or missing data in the original text, the researchers will contact the author to obtain the relevant data. The results of data extraction will be compared to exclude any differences, and any disagreement will be resolved by a third researcher (LX) or through discussion and consensus.

From all included studies, we will collect the following data:

1. Research and publication information, including the title, journal (volume, page number) or if unpublished, the author, year of publication, country, and setting, the language of publication, and funding sources;

2. Study design, including the type of design, inclusion criteria, exclusion criteria, randomization method (including concealment and blinding), and losses to follow up;

3. Characteristics of the subjects, including total sample size, number of participants in the intervention and control groups, gender, age, diagnosis, disease severity (Acute Physiology and Chronic Health Evaluation [APACHE] II scores), comorbidities, and mechanical ventilation status;

4. Intervention details, including type of music, control of music selection (by participant or researcher), the frequency, duration, and timing of music listening, and the format/devices used (e.g., headphone, loudspeaker); and

5. Outcomes, including the methods of assessment of sleep, anxiety, and depression, pre- and post-test means or change scores, and standard deviations.

Methodological quality assessment

The risk of bias and quality of the included studies will be evaluated using the Cochrane Collaboration's Risk for Bias tool, which evaluates seven sources of study bias: 1) random sequence generation, 2) allocation concealment, 3) performance bias, 4) detection bias, 5) incomplete outcome data, 6) selective reporting, and 7) other bias. Two researchers (LX and XL) will independently grade each element as ‘low risk’, ‘high risk’, or ‘unclear risk’[63]. Inconsistencies will be resolved through discussion and consensus, or by a third researcher (DH). For quality assessment of quasi-randomized controlled trials, an appropriate assessment will be completed.

Data synthesis and analysis

A meta-analysis will be conducted once there are a sufficient number of studies showing homogeneity. The statistical analysis will be performed using RevMan 5.3.5 software. Continuous data will be expressed with the odds ratio (OR) and its 95% confidence interval (CI). The level of heterogeneity of the included studies will be determined with the I2 statistic and P value[64]. If P>0.1 and I2<50%, suggesting no statistical heterogeneity, a meta-analysis will be performed using a fixed-effects model; if I2>50%, a random-effects model will be used to analyse the clinical heterogeneity. Subgroup analysis will be performed by: timing of intervention, type of intervention, severity of disease (APACHE II score <25, 25–35, >35), mechanical ventilation status (ventilated patients

versus non-ventilated patients), and study site (surgical ICU patients versus medical ICU patients). Sensitivity analysis will be used to determine the stability of the results, and Egger's regression test and funnel plots will be used to assess potential publication bias. If data pooling is not possible, quantitative data will be presented in a narrative review of the study primary and secondary outcomes, using thematic summaries and tables.

Validity and reliability /Rigour

The study protocol will use systematic review and meta-analytic methods, following the Cochrane Collaboration recommendations for performing a systematic review. The results will be reported according to the PRISMA-P guidelines[65]. Additionally, the CONSORT checklist will be used to examine the quality of the papers.

DISCUSSION

This paper presents the protocol for a systematic review of the literature examining the effects of music listening on sleep and psychological outcomes in critically ill patients. The study was undertaken to answer questions about the effectiveness of music listening in this population. Properly powered, intervention studies provide strong evidence, so this meta-analysis of the existing evidence will permit conclusions about the efficacy of music listening on sleep, anxiety, and depression in critically ill patients. Results from this project will provide recommendations for the use of music listening in this population and will support nurses and other health practitioners in their promotion of mental health. Additionally, by identifying existing lacunae in the literature, our results will prompt further research.

ETHICS AND DISSEMINATION

This work will review existing trial data and will not introduce new patient data or interventions. Thus, ethical committee approval is not required. This systematic review protocol will follow the PRISMA checklist. We will disseminate this protocol in a related peer-reviewed journal or at conferences.

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PRISMA 2009 Checklist

Section / topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	9
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	9
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	10
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	10

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	10
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

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Use of music to enhance sleep and psychological outcomes in critically ill patients: a protocol for systematic review and meta-analysis

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Use of music to enhance sleep and psychological outcomes in critically ill patients: a protocol for systematic review and meta-analysis

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Contributors

Lixia Chen, Fang Wang and Liang Wang were responsible for drafting the article or revising it critically for important intellectual content. Jianhua Li and Li Cui conducted final approval of the version to be submitted. Daihong Ji, Siqi Qu and Cuihua Han were responsible for the conception and design of the study, Xiaoli Liu supervised the work. All authors approved the final version of the article.

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Abstract

Introduction Music listening as a non-pharmacological intervention, is widely used in various populations with positive results, yet the evidence for music listening on sleep and psychological outcomes in critically ill patients is less clear. It is essential to better understand the impact of music listening for critically ill patients to optimise care and minimise risk of harm. We will assess whether music listening improves sleep and psychological outcomes in critically ill patients.

Methods and analysis We will systematically search scientific databases: PubMed, Embase, CINAHL, PsycINFO, Web of Science, Scopus, ProQuest, the Cochrane Central Register of Controlled Trials, China Biological Medicine Database, China National Knowledge Infrastructure Library, Wan fang databases, VIP Database for Chinese Technical Periodicals, and the Chinese Clinical Trial Registry. All databases will be searched for articles published from inception to 10 June 2020. Music therapy journals and reference lists in some articles will be hand-searched. Gray literature will also be searched. We will include randomized and quasi-randomized controlled trials of music listening to improve sleep and psychological outcomes in critically ill patients. The primary outcomes will be sleep-related outcomes, the secondary outcomes will be anxiety score, depression score and physiological outcomes. Two reviewers will independently verify study eligibility and methodological quality; disagreements will be resolved by a third reviewer or discussion. The risk of bias will be independently determined using the Cochrane Risk of Bias Tool. Data will be extracted from eligible studies by two researchers. RevMan (version 5.3) will be used for meta-analysis. Additionally, the CONSORT checklist will be used to examine the quality of the papers.

Ethics and Dissemination This work will review existing trial data and will not introduce new patient data or interventions, ethics committee approval is not required. We will disseminate this protocol in a related peer-reviewed journal.

PROSPERO Registration Number CRD42019147202

Strengths and limitations of this study

- We plan to employ robust international gold-standard methodology and comprehensive search strategy to reduce bias.
- We will assess the quality of the articles included using a validated tool.

- Subgroup analysis will be performed when possible to elaborate intervention or subject characteristics correlated with increased effectiveness.
- If there is high heterogeneity across studies, which may increase the difficulties to interpret a meta- analysis.
- Limited in that the systematic review protocol will only include articles in English and Chinese

INTRODUCTION

Rationale

Sleep disturbance is a frequent problem among patients in intensive care units (ICUs)[1 2]. Sleep quality and quantity[3] are negatively affected by the ICU environment (e.g., noise, lights), patient-care activities, symptoms of the patient's underlying illness, and by mechanical ventilation[4 5]. It is characterized by prolonged sleep onset latency, short sleep duration, frequent awakenings, non-restorative sleep, and decreased sleep efficiency (percentage of time in bed spent asleep). Sleep disturbance has been associated with numerous adverse consequences in critically ill patients, including impairments in immune function, memory, wound healing, and inspiratory muscle endurance; higher rates of delirium; and increased overall morbidity and mortality[6].

An increase in psychological problems, such as anxiety and depression, has also been found in critically ill patients[7 8]. One study[9] estimated that 70%–80% of critically ill patients suffer anxiety related to fear, sleeplessness, pain, discomfort, thirst, and disease-related symptoms; patients on assisted ventilation were especially prone to anxiety because of their need for frequent suctioning, inability to breath independently or talk, and general discomfort. It has also been found that one-half of patients experienced a high level of depression during the ICU stay[9]. In turn, unmanaged anxiety and depression have been associated with harmful effects on disease recovery and overall well-being: prolonged weaning from ventilation and recovery time[10], increased work of breathing, fatigue[11], and acute elevations in blood pressure[12], increase the depression incidence in ICU survivors[13]. Wewalka found that pre-existing depressive mood at the time of ICU admission was an independent risk factor for 28-day mortality in medical ICU patients[14].

Sufficient evidence showed that sleep disturbance, anxiety and depression were detrimental to their disease recovery and psychological well-being. Research has also reported the interplay of sleep disturbance, anxiety, and depression[15]. Anxiety and depression are both risk factors for sleep disturbance, and disturbed sleep pattern in turn increases emotional distress, leading to higher levels of anxiety and depression[16 17]. Therefore, nurses as key staffs in the ICU, need to provide effective interventions to address all of these.

Pharmacological and non-pharmacological interventions are proposed to manage sleep and psychological distress in the ICU. Pharmacological therapy is generally the first line of treatment[18 19]. However, pharmacological therapy itself has been associated with numerous adverse effects and

complications, including memory loss, prolongation of mechanical ventilation, altered sleep stages, longer length of hospitalization, tolerance, bradycardia, hypotension, residual daytime effects, dysmotility, weakness, and delirium[20 21]. Additionally, the medications used are expensive. To avoid this, a number of researchers have developed alternative, non-pharmacological therapies to improve sleep, anxiety, and depression in ICU patients, with positive results[22-24]. In recent years, the results of music intervention studies had led scientists to pay close attention to the relationship between music and sleep in various types of patients. This has resulted in an increase in the use of music therapy and music listening (sometimes called music medicine[25]).

Music can be defined as the organization of the tone over the time, it is one of the most pleasurable experiences for the human being. As far back as the early 1800s, Florence Nightingale[26] described the importance of music and its healing effect on patients, the music implemented in hospitals was live music. With the development of music discipline and science, more and more recorded music was used, music equipment used were mainly portable stereos, wall-mounted speakers, or mp3 player[27]. In medicine, music as a non-pharmacological be adopted by medical staff, the intervention involves different types of music, such as low volume, nature sounds, soothing music, Mozart piano, etc. It is relatively easy to implement, cost effective, safe and has no negative impacts[28]. Music therapy and music listening are common forms of music application that are similar but have distinct features. Music therapy is defined as the clinical and evidence-based use of music to realize individualized clinical goals within a therapeutic relationship. It is conducted by a certified music therapist, and centres on the dynamic musical interaction between the music therapist and the patient, verbal processing of the music experience, and implementation and alteration of music (tempo, volume, intensity) according to the patient's need[29 30]. The music therapy is consist of active and passive forms, active part refers to therapy needing patient participation in process, while passive part refers to therapy composing only of listening to music and without participation. But, no matter active or passive, music therapy is an evidence-based practice conducted by certified music therapists. In the course of therapy, music elements, such as melody, rhythm, tempo, harmony were considered by music therapists[31]. The use of environmental music therapy (EMT), which is a method within the field of music therapy, has been increasing in recent years[32 33]. EMT, involving live music to address a chaotic intensive care environment, helping to create a less tense atmosphere by trained, certified professionals. They apply live music to meet the psychological, physical and cultural needs

of caregivers, patients and staff in the hospital environment. Previous study have also verified the safety and effectiveness of EMT[34]. Music listening is defined as passive listening to recorded music via any form of music playback device (e.g. listening to a MP3 through earphones or a loudspeaker) or listening to live music, without interacting with a music therapist or theoretical framework. It can be provided by medical or healthcare professionals or self-administered by a patient, and patients may or may not be involved in selecting the music[35 36]. Although music-based application are used in both music listening and music therapy, it is important to distinguish the two interventions in clinical practice[37] due to the varying levels of training in the fundamentals of music and its therapeutic applications. For instance, music therapists receive specialized training in the aforementioned areas[25]. The effectiveness of music therapy is mostly caused by the active musical interaction between the patient and the music therapist, this is why numerous studies have indicated music therapy is more effective than music listening. However, most of the patients in ICU are critically ill and weak, patients may not have enough energy to interact with a music therapist. Music listening may be a preference, compared with music therapy, music listening could be used by more patients. And music listening has been widely used in various diseases, such as Parkinson disease[38], Alzheimer disease[39], and cancer[40], to assuage emotional, physiological, and psychological symptoms. A growing number of studies, in adults of all ages, have demonstrated the positive effects of music listening on anxiety, depression, stress, and pain[41 42], in various medical and surgical conditions. Repeated studies have specifically reported music listening improved sleep in critically ill patients[24 43 44]. Furthermore, music listening is inexpensive, relatively easy to carry out, and safe compared with pharmacological intervention[28], benefits that are favourably received by patients. Thus, music listening is a potentially viable alternative treatment option.

Clinical trials have provided support for the effectiveness of music application in the healthcare setting, psychophysiological theory[45] also provides clues to its mechanism of action. Music is made up of many key elements, including rhythm, pitch, harmony, and melody. These music elements play a comprehensive role in the degree to which music can promote sleep in patients[46]. Earlier authors described that sleep improvement is mediated by the relaxing, distracting effect of 'soothing' music[47]. Music with a slow tempo of 60–80 beats per minute mirrors the heart rate and reduces neuroendocrine and sympathetic nervous system activity, resulting in relaxation. Further, the peaceful atmosphere created by soothing music in the ICU setting is a mood enhancer, reducing

anxiety and depression, and lowering treatment-related stress. Elsewhere, other authors described the effect of music in modulating mood and emotions at the cortical level, through stimulation of self-image and intellect[48]. Clinical trials have also shown that listening to music reduced anxiety and stress responses—which can lead to greater relaxation and improvement of sleep[49 50].

Research on the impact of music listening for ICU patients has evolved during the past 20 years, several researchers studied the effects of music listening on sleep and psychological outcomes in critically ill patients. For example, recent studies reporting that music listening may improve stress, anxiety[8 51], depression[52] and sleep[53 54] in ICU patients. The intervention involves different types of music to improve sleep and psychological symptoms, such as low volume, nature sounds, soothing music, Mozart piano, etc. Music listening can be provided by specific tools (e.g. Mp3 or earphones or loudspeaker). The choice of music may be determined by the researcher or by participants themselves. The duration, frequency, and timing of music exposure has also varied among studies. Although clinical trials have been performed to investigate the effects of music listening on sleep and psychological outcomes, their safety and efficacy for critically ill patients have not been established. Most of these studies have suffered from small sample size[44 55], making it nearly impossible to achieve statistically significant results. The impact of the music listening may differ due to the different design of the intervention (study design, methods of intervention, and types of music). One systematic review have assessed the efficacy of music application for reducing anxiety in mechanically ventilated patients[36], the author only included mechanically ventilated patients. A recent systematic review also evaluated the effectiveness of music therapy to reduce stress and anxiety in critically ill patients[56]. In 2015, another review reported that music therapy appeared to be safe to improve sleep but did not do a meta-analysis, and further randomized controlled trials were required to assess efficacy[57]. The 2018 Pain, Agitation/ sedation, Delirium, Immobility (rehabilitation/mobilization), and Sleep (disruption) (PADIS) guideline also suggest no high quality evidence to prove that music could improve sleep in critically ill adults[1].

Until now, despite the large number of relevant studies, music listening has not been implemented as a therapeutic intervention in everyday critical care because information about effectiveness has not been synthesised and disseminated universally. So, we assess effectiveness of music listening in improvement of sleep, anxiety and depression in critically ill patients, and

investigate relevant subgroups (timing of intervention, type of intervention, severity of disease, mechanical ventilation status, and study site).

OBJECTIVES

This systematic review and meta-analysis aim to integrate the scientific research on the use of music listening to promote sleep, anxiety, and depression for critically ill patients in ICU. We attempt to answer the following research questions:

1.What are the effects of music listening on sleep quality and quantity in critically ill patients?

2.What are the effects of music listening on anxiety, depression and physiological outcomes in critically ill patients?

METHODS AND ANALYSIS

This is a quantitative systematic review protocol. We will follow the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines to complete and report the study protocol[58]. This systematic review protocol has been registered in PROSPERO (PROSPERO Registration Number CRD 42019147202)

Patient and public involvement

No patient and public involved in this study.

Inclusion/Exclusion criteria

Types of participants

Studies will be selected for inclusion if their subjects meet the criteria:

- adult patient in the ICU (age>18 years old),
- being conscious and clear (Glasgow Coma Scale score ≥14),
- ventilated or non-ventilated,
- admittance to the ICU ≥24 hours.

We will exclude studies whose subjects had:

- hearing damage,
- been diagnosed with / had overt signs or symptoms of obstructive sleep apnea,
- been diagnosed with dementia or neurologic disease,
- severe signs or symptoms of psychological illness, such as hallucinations, delusions, and

behavioral disorders, etc.

Types of intervention and comparison

We will include any study in which sleep or psychological variables were considered as outcomes of music listening combined with standard care vs. standard care alone or standard care with other interventions in critically ill patients.

Types of outcome measures

At least one of the following outcomes must have been reported in the study:

Primary outcomes

- Sleep outcomes
  1. Sleep quality
  2. Sleep onset latency
  3. Total sleep time
  4. Number of awakenings
  5. Sleep efficiency (percent of time in bed spent asleep)

Sleep outcomes are measured using a variety of methods. Subjective perception of sleep is measured through validated self-report tools, including the Richards–Campbell Sleep Questionnaire (RCSQ)[59], Pittsburgh Sleep Quality Index (PSQI)[60], and the Verran and Synder-Halpern (VSH) Sleep Scale[61]; objective measurement of sleep is done with polysomnography, actigraphy, bispectral index (BIS) monitoring, or electroencephalography (EEG).

Secondary outcomes

- Psychological outcomes
  1. Anxiety
  2. Depression

We will include trials that measured psychological outcomes using standardized questionnaires with established reliability and validity, including Hospital-based Anxiety and Depression Scales[62], the Visual Analogue Scale for Anxiety (VAS-A)[63], the Spielberger State-Trait anxiety Inventory[64], and the Beck Anxiety Inventory[65].

- Physiological outcomes (heart rate, blood pressure, respiratory rate)

Types of study designs

We will include any interventional study, including randomized and quasi-randomized controlled

trials.

Data source and search strategy

To identify eligible studies, we will search electronic databases, including: PubMed, Embase, CINAHL, PsycINFO, Web of Science, Scopus, ProQuest, the Cochrane Central Register of Controlled Trials, China Biological Medicine Database, China National Knowledge Infrastructure Library, Wang fang databases, VIP Database for Chinese Technical Periodicals, the Chinese Clinical Trial Registry. The databases will be searched from their start date to October 2020. Additionally, we will hand-search music therapy journals and the reference lists in some articles, as well as gray literature.

A health sciences librarian will design the search. Table 1 shows the search strategy, employing both keywords and Medical Subject Heading (MeSH) terms, that will be used to search PUBMED; this will be adapted for the other databases.

Table 1 Search strategy for PubMed

Filter: Humans
1 music [Mesh] OR 'music therapy' [Mesh] OR music medicine OR music* OR listen*
2 sleep [Mesh] OR sleep Disorders, Circadian Rhythm [Mesh] OR sleep* OR insomnia* OR wakeful* OR sleepless*
3 anxiety [Mesh] OR fear [Mesh] OR stress OR psychological OR depression [Mesh] OR depress* OR mood disorders [Mesh]
4 2 OR 3
5 critical illness [Mesh]) OR critical care [Mesh] OR 'intensive care units' [Mesh] OR ventilators, mechanical [Mesh] OR respiration, artificial [Mesh] OR intensive care OR ICU
6 **1 AND 4 AND 5**
7 infant* OR neonat* OR infant, premature [Mesh] OR infant, newborn [Mesh] OR Intensive Care Units, pediatric [Mesh]
8 6 NOT 7

Selection of studies

All articles retrieved through the search of the selected databases will be imported to Endnote, from which duplicate references will be removed. Two members of the research team (SQ and CH) will independently review the title/abstract of each article to verify each study meets the inclusion criteria; if a title or abstract is unclear, the two researchers will review the full article. Disagreements will be resolved by a third researcher (LX) or through discussion until consensus is reached. The reason for all exclusions will be recorded.

Data collection and validation

Two researchers (JH and CL) will independently extract data from the included studies, using the Cochrane Collaboration Data Collection Form[66]. In the event of questions or missing data in the original text, the researchers will contact the author to obtain the relevant data. The results of data extraction will be compared to exclude any differences, and any disagreement will be resolved by a third researcher (LX) or through discussion and consensus.

From all included studies, we will collect the following data:

1. Research and publication information, including the title, journal (volume, page number) or if unpublished, the author, year of publication, country, and setting, the language of publication, and funding sources;

2. Study design, including the type of design, inclusion criteria, exclusion criteria, randomization method (including concealment and blinding), and losses to follow up;

3. Characteristics of the subjects, including total sample size, number of participants in the intervention and control groups, gender, age, diagnosis, disease severity (Acute Physiology and Chronic Health Evaluation [APACHE] II scores), comorbidities, and mechanical ventilation status;

4. Intervention details, including type of music, control of music selection (by participant or researcher), the frequency, duration, and timing of music listening, and the format/devices used (e.g., headphone, loudspeaker); and

5. Outcomes, including the methods of assessment of sleep, anxiety, and depression, pre- and post-test means or change scores, and standard deviations.

Methodological quality assessment

The risk of bias and quality of the included studies will be evaluated using the Cochrane Collaboration's Risk for Bias tool[66], which evaluates seven sources of study bias: 1) random sequence generation, 2) allocation concealment, 3) performance bias, 4) detection bias, 5) incomplete

outcome data, 6) selective reporting, and 7) other bias. Two researchers (LX and XL) will independently grade each element as 'low risk', 'high risk', or 'unclear risk'[67]. Inconsistencies will be resolved through discussion and consensus, or by a third researcher (DH). For quality assessment of quasi-randomized controlled trials, an appropriate assessment will be completed.

Data synthesis and analysis

A meta-analysis will be conducted once there are a sufficient number of studies showing homogeneity. The statistical analysis will be performed using RevMan 5.3.5 software. Continuous data will be expressed with the odds ratio (OR) and its 95% confidence interval (CI). The level of heterogeneity of the included studies will be determined with the I^2 statistic and *P* value[68]. If $P>0.1$ and $I^2<50\%$, suggesting no statistical heterogeneity, a meta-analysis will be performed using a fixed-effects model; if $I^2>50\%$, a random-effects model will be used to analyse the clinical heterogeneity. Subgroup analysis will be performed by: timing of intervention, type of intervention, severity of disease (APACHE II score <25, 25–35, >35), mechanical ventilation status (ventilated patients versus non-ventilated patients), and study site (surgical ICU patients versus medical ICU patients). Sensitivity analysis will be used to determine the stability of the results, and Egger's regression test and funnel plots will be used to assess potential publication bias. If data pooling is not possible, quantitative data will be presented in a narrative review of the study primary and secondary outcomes, using thematic summaries and tables.

Validity and reliability /Rigour

The study protocol will use systematic review and meta-analytic methods, following the Cochrane Collaboration recommendations for performing a systematic review. The results will be reported according to the PRISMA-P guidelines[69]. Additionally, the CONSORT checklist will be used to examine the quality of the papers.

DISCUSSION

This paper presents the protocol for a systematic review of the literature examining the effects of music listening on sleep and psychological outcomes in critically ill patients. The study was undertaken to answer questions about the effectiveness of music listening in this population. Properly powered, intervention studies provide strong evidence, so this meta-analysis of the existing evidence will permit conclusions about the efficacy of music listening on sleep, anxiety, and

depression in critically ill patients. Results from this project will provide recommendations for the use of music listening in this population and will support nurses and other health practitioners in their promotion of mental health. Additionally, by identifying existing lacunae in the literature, our results will prompt further research.

ETHICS AND DISSEMINATION

This work will review existing trial data and will not introduce new patient data or interventions. Thus, ethical committee approval is not required. This systematic review protocol will follow the PRISMA checklist. We will disseminate this protocol in a related peer-reviewed journal or at conferences.

Competing interests None declared.

Reference

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PRISMA 2009 Checklist

3Section / topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	8
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	8
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8-9
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	10
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	10
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	11
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	11
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	11
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	12
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	12
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	12

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	12
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	12
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

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BMJ Open

Use of music to enhance sleep and psychological outcomes in critically ill patients: a protocol for a systematic review and meta-analysis

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Primary Subject Heading:	Intensive care
Secondary Subject Heading:	Intensive care, Mental health
Keywords:	Adult intensive & critical care < ANAESTHETICS, Sleep medicine < ANAESTHETICS, Adult intensive & critical care < INTENSIVE & CRITICAL CARE

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Use of music to enhance sleep and psychological outcomes in critically ill patients: a protocol for a systematic review and meta-analysis

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Contributors

Lixia Chen, Fang Wang, and Liang Wang were responsible for drafting the article and revising it critically for important intellectual content. Jianhua Li and Li Cui conducted final approval of the version to be submitted. Daihong Ji, Siqi Qu, and Cuihua Han were responsible for the conception and design of the study, Xiaoli Liu supervised the work. All authors approved the final version of the article.

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Abstract

Introduction: Music listening is used as a non-pharmacological intervention in various populations with positive results; however, evidence for its effect on sleep and psychological outcomes in critically ill patients remains unclear. It is essential to understand the impact of music listening for critically ill patients to optimize care and minimize the risk for harm. We will assess whether music listening improves sleep and psychological outcomes in critically ill patients.

Methods and analysis: We will systematically search scientific databases for relevant studies, including PubMed, Embase, CINAHL, PsycINFO, Web of Science, Scopus, ProQuest, the Cochrane Central Register of Controlled Trials, China Biological Medicine Database, China National Knowledge Infrastructure Library, Wan fang databases, VIP Database for Chinese Technical Periodicals, and the Chinese Clinical Trial Registry. Databases will be searched for articles published from inception to June 10, 2020. Music therapy journals and reference lists in some articles will be hand-searched. Gray literature will also be searched. We will include randomized and quasi-randomized controlled trials that used music listening to improve sleep and psychological outcomes in critically ill patients. The primary outcomes will be sleep-related outcomes, and secondary outcomes will be anxiety and depression scores and physiological outcomes. Two reviewers will independently verify study eligibility and methodological quality; disagreements will be resolved by a third reviewer or discussion. The risk of bias will be independently determined using the Cochrane Risk of Bias Tool. The CONSORT checklist will be used to examine the quality of included papers. Data will be extracted from eligible studies by two researchers. RevMan (version 5.3) will be used for meta-analysis.

Ethics and Dissemination: This work will review existing trial data and will not introduce new patient data or interventions; therefore, ethics committee approval is not required. We will disseminate this protocol in a related peer-reviewed journal.

PROSPERO Registration Number CRD42019147202.

Strengths and limitations of this study

- We plan to employ robust international gold-standard methodology and a comprehensive search strategy to reduce bias.
- We will assess the quality of included articles using a validated tool.

- Subgroup analyses will be performed when possible to elaborate intervention or participant characteristics correlated with increased effectiveness.
- High heterogeneity across studies may increase the difficulty in interpreting a meta-analysis.
- A limitation will be that the systematic review protocol will only include articles published in English and Chinese.

INTRODUCTION

Rationale

Sleep disturbance is a frequent problem among patients in the intensive care unit (ICU)[1 2]. Sleep quality and quantity are negatively affected by the ICU environment (e.g., noise, lights)[3], patient-care activities, symptoms of the patient's underlying illness, and mechanical ventilation[4 5]. In this context, sleep is characterized by prolonged sleep onset latency, short sleep duration, frequent awakenings, non-restorative sleep, and decreased sleep efficiency (percentage of time in bed spent asleep). Sleep disturbance has been associated with numerous adverse consequences in critically ill patients, including impairments in immune function, memory, wound healing, and inspiratory muscle endurance, along with higher rates of delirium and increased overall morbidity and mortality[6].

An increase in psychological problems (e.g., anxiety and depression) has also been found in critically ill patients[7 8]. One study[9] estimated that 70%–80% of critically ill patients experienced anxiety related to fear, sleeplessness, pain, discomfort, thirst, and disease-related symptoms. That study also reported patients on assisted ventilation were especially prone to anxiety because of their need for frequent suctioning, inability to breathe independently or talk, and general discomfort. In addition, around half of patients experienced a high level of depression during their ICU stay[9]. Unmanaged anxiety and depression have been associated with harmful effects on disease recovery and overall well-being, including prolonged weaning from ventilation and recovery time[10], increased work for breathing, fatigue[11], acute elevated blood pressure[12], and an increased depression incidence in ICU survivors[13]. Wewalka found that pre-existing depressive mood at the time of ICU admission was an independent risk factor for 28-day mortality among patients in the medical ICU[14].

Sufficient evidence shows that sleep disturbance, anxiety, and depression are detrimental to disease recovery and psychological well-being. Research has also reported an interplay of sleep disturbance, anxiety, and depression[15]. Anxiety and depression are both risk factors for sleep disturbance and disturbed sleep pattern increases emotional distress, which in turn lead to higher levels of anxiety and depression[16 17]. Therefore, as key ICU staff, nurses need to provide effective interventions to address these issues.

Pharmacological and non-pharmacological interventions are used to manage sleep and psychological distress in the ICU. Pharmacological therapy is generally the first-line treatment[18 19]. However, pharmacological therapy has been associated with numerous adverse effects and

complications, including memory loss, prolongation of mechanical ventilation, altered sleep stages, longer length of hospitalization, tolerance, bradycardia, hypotension, residual daytime effects, dysmotility, weakness, and delirium[20 21]. In addition, the medications used are expensive. To avoid these issues, researchers have developed alternative, non-pharmacological therapies to improve sleep, anxiety, and depression among patients in the ICU, and positive results have been reported[22-24]. The results of recent music intervention studies have drawn attention to the relationship between music and sleep in various patient groups. This resulted in increased use of music therapy and music listening (sometimes called music medicine[25]).

Music can be defined as the organization of tone over the time, and is one of the most pleasurable experiences for a human being. In the early 1800s, Florence Nightingale[26] described the importance of music and its healing effect on patients; the music first implemented in hospitals was live music. With the development of the music discipline and science, more recorded music was used and played to patients using musical equipment such as portable stereos, wall-mounted speakers, or devices such as Mp3 players[27]. Music as a non-pharmacological intervention has been adopted by medical staff, with these interventions involving different types of music, such as low volume, nature sounds, soothing music, and Mozart piano recordings. As an intervention, music is relatively easy to implement, cost effective, safe, and has no negative impacts[28]. Music therapy and music listening are common forms of music application that are similar but have distinct features. Music therapy is defined as the clinical and evidence-based use of music to realize individualized clinical goals within a therapeutic relationship. It is conducted by certified music therapists, and centers on the dynamic musical interaction between the music therapist and the patient, verbal processing of the music experience, and implementation and alteration of music (tempo, volume, intensity) according to the patient's needs[29 30]. Music therapy consists of active and passive forms. The active form refers to therapy that needs patient participation in the process, whereas the passive form refers to therapy that comprises listening to music without participation. Irrespective of whether it is active or passive, music therapy is an evidence-based practice conducted by certified music therapists. During therapy, music therapists consider elements of music such as melody, rhythm, tempo, and harmony[31]. The use of environmental music therapy (EMT), which is type of music therapy, has increased in recent years[32 33]. EMT involves trained, certified professionals using live music to address a chaotic intensive care environment and help to create a less tense atmosphere. They apply live music to meet

the psychological, physical, and cultural needs of caregivers, patients, and staff in the hospital environment. A previous study verified the safety and effectiveness of EMT[34].

Music listening is defined as passive listening to recorded music via any form of music playback device (e.g., earphones or speakers) or listening to live music without interacting with a music therapist or theoretical framework. It can be provided by medical or healthcare professionals or self-administered by a patient, and patients may or may not be involved in selecting the music[35 36]. Although music-based applications are used in both music listening and music therapy, it is important to distinguish the two interventions in clinical practice[37] because of the varying levels of training in the fundamentals of music and its therapeutic applications. For example, music therapists have received specialized training in the aforementioned areas[25]. The effectiveness of music therapy is mostly attributable to the active musical interaction between the patient and the music therapist, which is why numerous studies suggest music therapy is more effective than music listening. However, most patients in the ICU are critically ill and weak, and may not have enough energy to interact with a music therapist. Music listening may therefore be preferred, as compared with music therapy, it may be used by more patients. Music listening has also been widely used to assuage emotional, physiological, and psychological symptoms in various diseases, such as Parkinson's disease[38], Alzheimer's disease[39], and cancer[40]. A growing number of studies involving adults of all ages with various medical and surgical conditions have demonstrated the positive effects of music listening on anxiety, depression, stress, and pain[41 42]. Repeated studies have specifically reported music listening improved sleep in critically ill patients[24 43 44]. Furthermore, music listening is inexpensive, relatively easy to implement, and safe compared with pharmacological interventions[28]; these benefits are favorably received by patients. Therefore, music listening is a potentially viable alternative treatment option.

Clinical trials have provided support for the effectiveness of the application of music in the healthcare setting. Psychophysiological theory[45] also provides clues to its mechanism of action. Music comprises many key elements, including rhythm, pitch, harmony, and melody. These elements play a comprehensive role in the degree to which music can promote sleep in patients[46]. Previous authors described that sleep improvement is mediated by the relaxing, distracting effect of "soothing" music[47]. Music with a slow tempo (e.g., 60–80 beats per minute) mirrors the heart rate and reduces neuroendocrine and sympathetic nervous system activity, resulting in relaxation.

Furthermore, the peaceful atmosphere created by soothing music in the ICU setting is a mood enhancer, reduces anxiety and depression, and lowers treatment-related stress. Other authors described the effect of music in modulating mood and emotions at the cortical level through stimulation of self-image and intellect[48]. Clinical trials have also shown that listening to music reduced anxiety and stress responses, which can lead to greater relaxation and improved sleep[49 50].

Research on the impact of music listening for patients in the ICU has evolved over the past 20 years, and several researchers have studied the effects of music listening on sleep and psychological outcomes in critically ill patients. For example, recent studies reported that music listening may improve stress, anxiety[8 51], depression[52], and sleep[53 54] in ICU patients. As an intervention, music listening involves using different types of music to improve sleep and psychological symptoms (e.g., low volume, nature sounds, soothing music, classical music). Music listening can be provided by specific tools (e.g., Mp3 format via earphones or loudspeaker). The choice of music may be determined by the researcher or by participants themselves. The duration, frequency, and timing of music exposure has also varied among studies. Although clinical trials have been performed to investigate the effects of music listening on sleep and psychological outcomes, their safety and efficacy for critically ill patients have not been established. In addition, most of these studies used small sample sizes[44 55], making it nearly impossible to achieve statistically significant results. The impact of music listening may also differ because of different intervention designs (study design, method of intervention, and type of music). A previous systematic review assessed the efficacy of music application for reducing anxiety among mechanically ventilated patients[36], but only included mechanically ventilated patients. A recent systematic review also evaluated the effectiveness of music therapy to reduce stress and anxiety in critically ill patients[56]. In 2015, another review reported that music therapy appeared to be safe to improve sleep; however, that study did not perform a meta-analysis and noted further randomized controlled trials were required to assess efficacy[57]. The 2018 Pain, Agitation/sedation, Delirium, Immobility (rehabilitation/mobilization), and Sleep (disruption) (PADIS) guideline also suggests there is no high-quality evidence to prove that music could improve sleep in critically ill adults[1].

Despite the large number of relevant studies, music listening has not been implemented as a therapeutic intervention in everyday critical care because information about its effectiveness has not been synthesized and disseminated universally. Therefore, we aim to assess the effectiveness of

music listening in improving sleep, anxiety, and depression in critically ill patients, and investigate relevant subgroups (i.e., timing of intervention, type of intervention, severity of disease, mechanical ventilation status, and study site).

OBJECTIVES

This systematic review and meta-analysis aims to integrate available scientific research on the use of music listening to promote sleep and reduce anxiety and depression for critically ill patients in the ICU. We will attempt to answer the following research questions.

1. What are the effects of music listening on sleep quality and quantity in critically ill patients?
2. What are the effects of music listening on anxiety, depression, and physiological outcomes in critically ill patients?

METHODS AND ANALYSIS

This paper presents a quantitative systematic review protocol. We will follow the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines to complete and report the study protocol[58]. This systematic review protocol has been registered in PROSPERO (PROSPERO Registration Number CRD 42019147202).

Patient and public involvement

There is no patient or public involvement in this study.

Inclusion/exclusion criteria

Types of participants

Studies will be selected for inclusion if their participants meet specific criteria:

- adult patients in the ICU (aged ≥18 years),
- conscious and clear (Glasgow Coma Scale score ≥14),
- ventilated or non-ventilated,
- admitted to the ICU ≥24 hours.

We will exclude studies that included participants with:

- hearing damage,
- a diagnosis of or overt signs or symptoms of obstructive sleep apnea,
- a diagnosis of dementia or neurologic disease,

- severe signs or symptoms of psychological illness, such as hallucinations, delusions, and behavioral disorders.

Types of intervention and comparison

We will include any study that considered sleep or psychological variables as outcomes of music listening combined with standard care versus standard care alone or standard care with other interventions in critically ill patients.

Types of outcome measures

At least one of the following outcomes must have been reported in the study.

Primary outcomes

- Sleep outcomes
  1. Sleep quality
  2. Sleep onset latency
  3. Total sleep time
  4. Number of awakenings
  5. Sleep efficiency (percent of time in bed spent asleep)

Sleep outcomes may be measured using a variety of methods. Subjective perception of sleep is measured through validated self-report tools, including the Richards–Campbell Sleep Questionnaire[59], Pittsburgh Sleep Quality Index[60], and the Verran and Synder-Halpern Sleep Scale[61]. Objective measurement of sleep is performed with polysomnography, actigraphy, bispectral index monitoring, or electroencephalography.

Secondary outcomes

- Psychological outcomes
  1. Anxiety
  2. Depression

We will include trials that measured psychological outcomes using standardized questionnaires with established reliability and validity, including Hospital-based Anxiety and Depression Scales[62], the Visual Analogue Scale for Anxiety[63], the Spielberger State-Trait Anxiety Inventory[64], and the Beck Anxiety Inventory[65].

- Physiological outcomes (heart rate, blood pressure, respiratory rate)

Types of study designs

We will include any interventional study, including randomized and quasi-randomized controlled trials.

Data source and search strategy

To identify eligible studies, we will search electronic databases, including PubMed, Embase, CINAHL, PsycINFO, Web of Science, Scopus, ProQuest, the Cochrane Central Register of Controlled Trials, China Biological Medicine Database, China National Knowledge Infrastructure Library, Wang Fang databases, VIP Database for Chinese Technical Periodicals, and the Chinese Clinical Trial Registry. These databases will be searched from inception to June 10, 2020. In addition, we will hand-search music therapy journals and the reference lists of relevant articles, as well as gray literature.

A health sciences librarian will design the search. Table 1 shows the search strategy with both keywords and Medical Subject Heading terms that will be used to search PubMed; this strategy will be adapted as appropriate for other databases.

Table 1. Search strategy for PubMed

Filter: Humans
1 music [Mesh] OR 'music therapy' [Mesh] OR music medicine OR music* OR listen*
2 sleep [Mesh] OR sleep Disorders, Circadian Rhythm [Mesh] OR sleep* OR insomnia* OR wakeful* OR sleepless*
3 anxiety [Mesh] OR fear [Mesh] OR stress OR psychological OR depression [Mesh] OR depress* OR mood disorders [Mesh]
4 2 OR 3
5 critical illness [Mesh]) OR critical care [Mesh] OR 'intensive care units' [Mesh] OR ventilators, mechanical [Mesh] OR respiration, artificial [Mesh] OR intensive care OR ICU
6 **1 AND 4 AND 5**
7 infant* OR neonat* OR infant, premature [Mesh] OR infant, newborn [Mesh] OR Intensive Care Units, pediatric [Mesh]
8 6 NOT 7

Selection of studies

All articles retrieved through the search of the selected databases will be imported into Endnote, and duplicate references will be removed. Two members of the research team (SQ and CH) will independently review the title/abstract of each article to verify that each study meets the inclusion criteria. If a title or abstract is unclear, the two researchers will review the full article. Disagreements will be resolved by a third researcher (LX) or through discussion until consensus is reached. The reasons for all exclusions will be recorded.

Data collection and validation

Two researchers (JH and CL) will independently extract data from the included studies using the Cochrane Collaboration Data Collection Form[66]. In the event of questions about or missing data in the original text, the researchers will contact the authors to obtain the relevant data. The results of data extraction will be compared to exclude any differences, and any disagreement will be resolved by a third researcher (LX) or through discussion and consensus.

From all included studies, we will collect the following data.

1. Research and publication information, including the title, journal (volume, page number) or if unpublished, the author, year of publication, country, setting, language of publication, and funding sources.

2. Study design, including the type of design, inclusion criteria, exclusion criteria, randomization method (including concealment and blinding), and loss to follow up.

3. Characteristics of the participants, including total sample size, number of participants in the intervention and control groups, gender, age, diagnosis, disease severity (Acute Physiology and Chronic Health Evaluation [APACHE] II scores), comorbidities, and mechanical ventilation status.

4. Intervention details, including type of music, control of music selection (by participant or researcher), the frequency, duration, and timing of music listening, and the format/devices used (e.g., headphone, loudspeaker).

5. Outcomes, including the methods of assessment of sleep, anxiety, and depression, pre- and post-test means or change scores, and standard deviations.

Methodological quality assessment

The risk of bias and quality of the included studies will be evaluated using the Cochrane Collaboration Risk of Bias Tool[66], which evaluates seven sources of study bias: 1) random sequence generation, 2) allocation concealment, 3) performance bias, 4) detection bias, 5) incomplete outcome

data, 6) selective reporting, and 7) other bias. Two researchers (LX and XL) will independently grade each element as low risk, high risk, or unclear risk[67]. Inconsistencies will be resolved through discussion and consensus, or by a third researcher (DH). An appropriate assessment will be completed for the quality assessment of quasi-randomized controlled trials.

Data synthesis and analysis

A meta-analysis will be conducted when there are sufficient studies showing homogeneity. Statistical analyses will be performed using RevMan 5.3.5 software. Continuous data will be expressed with odds ratios and 95% confidence intervals. The level of heterogeneity of the included studies will be determined with the I^2 statistic and *P*-value[68]. If there is statistical heterogeneity ($P>0.1$ and $I^2<50\%$), a meta-analysis will be performed using a fixed-effects model. A random-effects model will be used to analyze clinical heterogeneity if $I^2>50\%$. Subgroup analyses will be performed by timing of intervention, type of intervention, severity of disease (APACHE II score <25, 25–35, >35), mechanical ventilation status (ventilated patients vs. non-ventilated patients), and study site (surgical ICU patients vs. medical ICU patients). Sensitivity analyses will be used to determine the stability of the results, and Egger's regression test and funnel plots will be used to assess potential publication bias. If data pooling is not possible, quantitative data will be presented in a narrative review of the study primary and secondary outcomes using thematic summaries and tables.

Validity and reliability/rigor

The study protocol will use systematic review and meta-analytic methods and follow the Cochrane Collaboration recommendations for performing a systematic review. The results will be reported according to the PRISMA-P guidelines[69]. In addition, the CONSORT checklist will be used to examine the quality of the included papers.

DISCUSSION

This paper presents the protocol for a systematic review of the literature examining the effects of music listening on sleep and psychological outcomes among critically ill patients. The study will be undertaken to answer questions about the effectiveness of music listening in this population. Properly powered, intervention studies provide strong evidence; therefore, this meta-analysis of existing evidence will permit conclusions about the efficacy of music listening on sleep, anxiety, and depression among critically ill patients. Results from this study will provide recommendations for the

use of music listening in this population and support nurses and other health practitioners in their promotion of mental health. In addition, by identifying existing lacunae in the literature, our results will prompt further research.

ETHICS AND DISSEMINATION

This work will review existing trial data and will not introduce new patient data or interventions; therefore, ethical committee approval is not required. This systematic review protocol will follow the PRISMA checklist. We will disseminate this protocol in a related peer-reviewed journal or at conferences.

Competing interests None declared.

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PRISMA 2009 Checklist

3Section / topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	8
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	8
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8-9
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	10
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	10
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	11
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	11
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	11
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	12
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	12
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	12

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	12
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	12
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

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