Aus dem Institut für Gesundheits- und Pflegewissenschaft an der Medizinischen Fakultät der Martin-Luther-Universität Halle-Wittenberg
(Direktorin: Prof. Dr. Gabriele Meyer)

The effect of music on sleep disorders
A systematic review and meta-analysis

Die Wirkung der Musik auf Schlafstörungen
Eine systematische Übersichtsarbeit und Metaanalyse

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von Aichen Huang, geb. Chou

geboren am 3. Februar 1985 in Taitung, Taiwan

Betreuer: PD Dr. Gero Langer

Gutachterin/Gutachter:

Prof. Dr. med. Michael Bucher
Prof. Dr. Sascha Köpke, Kiel
PD Dr. Gero Langer

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Referat

Die Wirkung von Musik auf den Menschen mit Schlafstörungen ist jahrelang bekannt. In einigen Arbeiten wurde bereits der Einfluss von Musik auf Schlafstörungen nachgewiesen. Allerdings fehlen noch klinische Indikationen bei der Anwendung von Musik. Mit einer erweiterten Sicht liegt das Forschungsziel überwiegend darin, die Wirkung der Musik auf verschiedenartige Schlafstörungen bzw. auf unterschiedlichen Gruppen von Patienten mit Schlafproblemen zu überprüfen. Eine Übersichtsarbeit mit Metaanalyse wurde durchgeführt. Eingeschlossen wurden Patienten mit einer Diagnose von Insomnie, schlafbezogener Atemstörung sowie schlafbezogener Epilepsie (gemäß ICSD-III/ ICD-10/ DSM-V); ebenfalls wurden Patienten auf der Intensivstation oder vor/nach einer Operation mit Schlafbeschwerden (unabhängig von einer gesicherten Insomnie) sowie die Frühgeborenen mit gestörter Schlafentwicklung einbezogen. Die Recherche erfolgte in einschlägigen Datenbanken ohne Sprachbeschränkung. GRADE Kriterien wurden bei der Einschätzung der Evidenz eingesetzt. Insgesamt wurden 29 qualifizierte Studien mit 2013 Patienten eingeschlossen, die nach den variierten klinischen Zuständen in drei Gruppen eingeteilt wurden: (1) Insomnie, (2) Schlafbeschwerden auf der Intensivstation oder vor/nach einer Operation und (3) spezifische Anwendungen der Musik auf andere schlafbezogene Probleme. Mit einer niedrigen bis moderaten Heterogenität zeigte sich das Ergebnis einheitlich in verschiedenen Subgruppen. Zusammenfassend verbesserte sich die subjektive Schlafqualität der Patienten mit Depression, chronischen Schmerzen sowie unspezifisch bedingter Insomnie, insbesondere war die Effektstärke bei Tumorpatienten erheblich. Weiterhin zeigte sich eine signifikante Verbesserung der Schlafqualität bei Patienten auf Intensivstation oder vor/nach einer Operation nach einer kurzfristigen Behandlung 1-3 Tage. Biologische Veränderungen (z.B. die Verlängerung der Tiefschlafphase und REM-Schlafdauer, die Verkürzung der Einschlafphase) wurden durch den Einsatz von 1-4 Tage Musikhören zum Teil hervorgerufen. Zur Reduzierung Epileptischer Aktivität, Minderung schlafbezogener Atemstörung und Unterstützung frühgeborener Schlafentwicklung wurden die Effekte von Musik positiv in einigen einzelne Studien gesehen. Als eine schonende, praktische, günstige und sichere Methode empfiehlt sich der Musikeinsatz für die klinische Behandlung der Schlafstörungen. In der Zukunft wünscht man sich eine verbesserte Studienqualität, um eine präzisere Weiterarbeit zu erzielen. Des Weiteren könnten die musikalischen Faktoren detailliert dargestellt und deren Einfluss bei verschiedenen Krankheitsbildern untersucht werden. Infolgedessen könnten die Richtlinien zur klinischen Behandlung und weiter zur Dosierung musikalischer Anwendungen gezielter erstellt werden.

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LIST OF ABBREVIATIONS

A&HCI	Arts & Humanities Citation Index
aEEG	Amplitude-integrated EEG
BDI	Beck Depression Inventory
BSID	Bayley Scales of Infant Development
CCU/ICU	Critical Care Unit/Intensive Care Unit
Chi^2	Chi-squared test
CJFD	China Academic Journals Full-text Database
DMDI	Deutsches Institut für Medizinische Dokumentation und Information
DSM	Diagnostic and Statistical Manual of Mental Disorders
ECG	Electrocardiography
EEG	Electroencephalography
EMG	Electromyography

EOG	Electrooculography
GDT	Guideline Development Tool
GIM	Guided Image and Music
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
ICSD	International Classification of Sleep Disorders
IPSA	International Pediatric Sleep Association
MADRS	Montgomery Asberg Depression Rating Scale
MD	Mean Difference
MeSH	Medical Subject Headings
NBAS	Neonatal Behavioural Assessment Scale
NICU	neonatal Intensive Care Unit
NREM	Non-rapid Eye Movement Sleep (including stage 1-4)
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analyses
PSG	Polysomnography
PSQI	Pittsburgh Sleep Quality Index
QE	Test of Residual Heterogeneity
QM	Test of Moderators
RCSQ	Richards-Campbell Sleep Questionnaire
REM	Rapid Eye Movement Sleep
RevMan	Review Manager
SAS	Self-Rating Anxiety Scale
SCI-Expanded	Science Citation Index Expanded
SCL 90	Symptom Checklist-90
SCN	Suprachiasmatic nucleus
SDS	Self-Depression Scale
SE	Sleep Efficacy
SE	Standard Error
SMD	Standard Mean Difference
SOL	Sleep Onset latency
SSCI	Social Sciences Citation Index
STAI	State-Anxiety Inventory
TST	Total Sleep Time
VAS	Visual Analogue Scale for pain
VRS	Verbal Rating Scale for pain
VSH	Verran and Snyder-Halpern
WASM	World Association of Sleep Medicine
WASO	Wake After Sleep Onset
WMD	Weighted Mean Difference

1 Introduction

1.1 Background of sleep problems

Many people have suffered from sleeping problems such as having difficulty in falling asleep, waking up at midnight, or feeling sleepy and fatigued during the daytime. Both poor sleep quality and daytime sleepiness can reduce our energy, productivity, bring about negative emotion, and even damage our mental and physical well-being. Sleep disorders affects people worldwide. According to epidemiological studies, about 30% of adults reported insomnia problem as long as one year, about 10% of adults reported chronic insomnia, and about 9-21% of women and 24-31% of men often complained about sleep-related respiratory difficulties [1]. Another study reported that approximately 4.8 million German people have persistent trouble with sleep; 2-3 million suffer from sleep-related breathing disorders (sleep apnea); 1-2 million refer to restless legs syndrome (RLS); over one million depend on sleeping pills [2]. More details have been added by Robert Koch-Institute: around 30.3% of adults are often tortured by nighttime sleep difficulty at least 3 times a week, among which 21.9% complained about insufficiency of sleep quality and 5.7% had daytime dysfunctions or distress owing to sleep difficulty [3]. The relative risk factors for sleep disorders are multi-dimensional and associated with increasing age, gender, distress, living style, lower socioeconomic status, working night or rotating shifts, comorbid medical conditions, physical and mental disorders [3, 4]. Commonly insomnia symptoms appear among females more than among males, with a ratio of about 1.44:1 [5].

Various kinds of sleep disorders have been thoroughly categorized in the two representative classification systems - ICSD (International classification of sleep disorders) and DSM (Diagnostic and Statistical Manual of Mental Disorders), in which a principle guideline of diagnosis has been instructed [5, 6]. Moreover, they provide an overview of sleep disorders and their important definitions. In the introduction of this current study, some types of sleep disorders that have been studied by means of music-based intervention are discussed in the following paragraphs: insomnia and sleep apnea as two common forms of sleep disorders are described firstly in detail; secondly, the general sleep disturbances in some specified conditions are mentioned as well. For instance, the patients in critical care unit usually have predictable sleep problem, but their sleep-related diagnose could not be established in advance. Subsequently, as a special part, sleep development in preterm-infants is delineated as well.

1.1.1 Insomnia

Insomnia is the most prevalent form of sleep disorders. In spite of various races, cultures and countries, most people have complained of insufficient sleep in a certain time period. Some of them might even become a chronic sleep difficulty, which may bring about several forms of daytime dysfunction, such as fatigue, mood disturbance, attention impairment etc.. According to ICSD-3 and DSM-5, the general definition of insomnia indicates that the complaint about difficulty initiating sleep and maintaining sleep occurs in despite of adequate sleep opportunity, accompanying the daytime impairments. Insomnious symptoms should be observed in the past three months and then persistent at least three times a week or more frequently. On this basis, a diagnosis of chronic insomnia could be made. Further, it is recommended in ICSD-3 that the probable comorbidities should be taken into account for identifying the certain causation of insomnia [7]. Besides, DSM-V indicates that the clinical insomnia should be distinguished from the age-related sleep changes or sleep deprivation due to inadequate circumstances [8]. The differential categories of insomnia are allowed to state, such as short-term insomnia disorder (if the 3-month duration is not met) or other insomnia disorder [5].

In the view of biological mechanism, the pathology of sleep disorders is connected to several physical and psychical factors, which cause the change of the cycle of sleep and wakefulness. This cycle is known as circadian rhythms (generally called an internal biological clock). Concerning the neurological understanding this circadian rhythms are regulated by suprachiasmatic nucleus (SCN) located in hypothalamus region [9]. An indicator of abnormal SCN is common to the people with mental disorders as well as to the people with neurological disorders, such as Alzheimer's disease, Parkinson’s disease, and brain injury. In these clinical conditions, insomnia occurs either as a complication or a comorbidity [4]. Indeed, insomnia as comorbid diagnosis happens very often in people with different medical statuses; for instance, chronic insomnia is frequently associated with psychiatric disorders, chronic pain disorders, and cancer patients. As the research demonstrated, about 40% of insomniacs are accompanied by other mental illnesses concurrently, e.g. depression, mood disturbance [10].

Patients with insomnia generally receive pharmacological treatment. In fact, it could heal the symptom rapidly, but as a long-term intervention, it could lead to side effects and problems after quitting medication. Therefore, the researcher has put the special emphasis on alterative and complementary therapies for insomnia in the past decade. For example, cognitive behavioral therapy is widely used to treat insomnia. Light therapy is recommended to reduce disturbance of jet lag. Melatonin is currently provided to regulate circadian rhythms [11]. However, the side effect of Melatonin has not been known completely yet. Furthermore, relaxation techniques, stimulus control therapy, and sleep hygiene are often introduced to help a person in establishing a bedtime ritual before sleep, changing environmental inferences as well as restricting sleep procedures.

In order to obtain a certain diagnosis, the individual history of sleep and the habit of sleep must be documented. Once a patient was regarded as insomnia, a validated sleep assessment, e.g. ESS, ISI, PSQI, may be quite useful for an initial estimate. On the one hand, those insomnia assessments indicate the subjective quality of sleep; on the other hand, it is still crucial to have the objective evaluation. Hence, the Polysomnography (PSG) has been used popularly in the sleep research. Through PSG monitors, the multiple biological indicators can be measured during sleep, including the activity of brain (EEG), of eye movements (EOG), of muscle (EMG), and heart rate (ECG). Those quantitative data responding to human sleep in different stages are recorded as the sleep architecture, which supports an individual diagnosis and its pathology. Both objective and subjective measurements provide the more comprehensive evidence for clinical decision making and management of the patients.

1.1.2 Sleep-related breathing disorder (sleep apnea)

Sleep apnea is the other usual form of sleep disorder. It manifests among 2%-15% adults in middle-age, over 20% in elderly people, and about 1%-2% in children [5]. Sleep apnea occurs most commonly with loud snoring, which can be observed since childhood and may be more serious with increasing age. In addition to snoring, the typical diagnostic criterion include fatigue, sleepiness, difficulty initiating or maintain sleep, awakening short of breath, and witnessed apneas. The term "witnessed apneas" usually refers to the correlative partner's report. Moreover, the diagnosis requires the certain evaluation of PSG measure, which can provide more concrete evidences of patients suffering from predominantly obstructive respiratory and/or hypopnea (an abnormally respiratory rate). More details about the types of sleep apnea and diagnosis criterion are defined in the ICSD-III and DSM-V. Furthermore, sleep-related breathing disorder may be associated with several medical and psychiatric disorders, such as hypertension, diabetes, obesity, coronary artery disease, congestive heart failure, stroke, cognitive dysfunction, and anxiety [12–15]. The most interesting is the patients with suspected obstructive sleep apnea report their quality of life more respondent to the level of sleep quality than respondent to breathing obstacle during sleep [16]. The effective treatments of sleep apnea involved continuous sleep airway pressure therapy and oral appliance (mandibular advancement device). Indeed, those approaches result in reducing daytime sleepiness and cardiovascular morbidity, even minimizing the mortality in patients with severe sleep apnea (episodes > 30 / h) [17–19].

1.1.3 Sleep disturbances in CCU/ICU

In addition to the certain diagnosis of sleep disorders, sleep disturbances could be usually predicted in some specified conditions, such as during surgery-related treatment, during staying in critical care unit/intensive care unit (CCU/ICU) as well. In those conditions, the sleeping problem might last until a chronic insomnia disorder is made, regardless of the absence of initial stimuli. Recently, many clinical studies have documented the sleep problems in intensive care unit with polysomnographic evidences, which indicated the decreased total sleep time, increased arousals and NREM stage 1&2, a lower percentage of slow-wave sleep as well as REM sleep [20–22]. The pool sleep in ICU is strongly caused by noise, pain, and care activities such as monitoring of vital signs. Moreover, the most medications provided may negatively affect sleep quality and architecture, e.g. propofol, benzodiazepines. Though some of them can extend the total sleep time, the multiple medications may affect the neurotransmitter balance, leading to the suppression of the deep sleep (slow-wave sleep) and REM sleep [23]. Another study has given the evidence about sleep disturbance after intensive care, in which about 50% patients reported moderate to severe sleep problems after hospital discharge of one week; nearly one third of respondents maintained moderate to severe sleep problems in a half year [24, 25]. Hence, a beneficial planning of treatment for improving sleep quality and preventing an insomnia-related disorder in such patients becomes an important challenge currently for physicians and researchers.

1.1.4 Sleep problem in preterm-infants

Sleeping and waking patterns in preterm infants may directly reflect the development of brain, which is regarded as the center responding to stimulation. Previous studies have indicated that the abnormality of sleep-wake behaviors in preterm infants may continue after NICU discharge, even occur in the further stages of the infants' growing development [26]. Besides, preterm infants are more likely to suffer from neurological problems including cognitive delays and epilepsy, which may cause several developmental issues consequently. Normally, the developmental status of premature children strongly depends on the change of active sleep with rapid eye movements. Another sleep problem showed in several studies is the sleep-related breathing disorder. It was indicated that people born prematurely had a greater risk of sleep-related breathing problem than other people born in full-term [27]. Therefore, the treatment in NICU is targeted at regulating a healthy pattern of sleep-wake as well as moderating the mood disturbances.

Most measurements of sleep quality in premature infants usually require clinical observation of infant behavior. The rating scales for caregivers are commonly used in NICU, such as Neonatal Behavioural Assessment Scale (NBAS) [28], Bayley Scales of Infant Development (BSID) [29].

1.2 Music intervention

In the past decades, music intervention has been applied in various clinical fields, such as psychiatry, psychological therapy, relief of pain, tinnitus, reduction of anxiety, and relaxation training. As a kind of noninvasive treatment, music has been testified to its advantage for health care. One of well-known effects on mentality is to modulating mood, that is generally used to alleviate anxiety and depression. Undoubtedly, music has made a valuable contribution to human emotion responding to a serial of neural based interactions, such as autonomic nervous system, the hormonal, and the immune system [30]. The immune system known from biological research interacts closely with body's sleep control. The limbic system is often evoked as well, due to emotional experience in music [31] ; even brain wave could be influenced by some particular music pieces as well. For instance, Morzart's Sonata K. 448 had been explored in the patients with epilepsy. This result indicated that the significant reduction of seizure frequency occurred after listening to music for one year and the sleep quality of patients was promoted accordingly [32]. In another brain research, Mozart's Divertimento K. 205 was examined as effective to produce dopamine in human brain and thus reduced blood pressure in various patients [33]. In a study of schizophrenia, music intervention added to standard care achieved a better therapeutic effect than standard care alone [34, 35]. Music has also been proved to suppress the symptoms of mental disorders in the treatment duration 1-3 months with at least 10 music therapy sessions [11, 36–38]. For patients before or after surgery, music improved the quality of sleep in the first 3 days; meanwhile, pain and anxiety were reduced as well [1, 39]. In addition to relieve chronic and acute pain, music facilitates relaxation of muscle and harmonizes the organic network, so that the restoration of healthy can be achieved [40–42].

Music intervention includes active and perceptive characteristics. The former is related with playing musical instruments or singing; the latter focuses on particularly listening to music. Music intervention is mostly beneficial to self-help strategies due to its safe, inexpensive and easily available properties. So far as the music intervention is concerned, the entity of music is likely manifested by different music parameters involving tempo, rhythms, pitch, timbre and melody. They can facilitate the synchronization of human body in many aspects, such as regulation of respiration, heart rate, blood pressure, and even in neurological rehabilitation, e.g. gait training, which is the most prominent approach [43]. Besides, music with tempo 60 bpm is similar to human heart rate in the stage of falling asleep; thus, it has been proposed to moderate the heart rate before bed time [44].

Furthermore, music relaxation program can assist elderly people not merely in better falling asleep, but also in strengthening daytime function [45]. Moreover, music has been united recently to cancer treatment and postoperative patients owing to its positive influence on the patients' psychological and physical outcomes [46, 47]. Music could increase the enjoyment, albeit several studies showed inconsistent results in the music effect on life-quality [47, 48]. Sleep can be a health indicator of neurological development in the premature infant; therefore the recorded music is suggested to the neonatal intensive care unit (NICU) for improving sleep condition and remaining a sound sleep [49].

1.3 Music in sleep research concerning the updated knowledge

Owing to the potentials of music, it has currently been applied to patients with insomnia symptoms. The first representative review article for music effect on sleep disorders was published in 2009, in which it was noted that music-assisted relaxation has the potential ability to promote sleep quality in patients with sleep disturbance [50]. The usage of music can create a more comfortable environment and thus can affect the psychological arousal for inducing NREM 1 sleep before going to bed. This study retrieved the potential reports from the initial date to 2008.

There were five studies finally included in a meta-analysis, in which a subgroup-analysis was conducted according to whether the measurement of relaxation was present, showing no significance between subgroups. Besides, follow-up length was explored in its correlation to effect size, resulting in no significance. Although this study concluded the benefit of music-assisted relaxation for sleep quality, the heterogeneity was not comprehensive yet.

Another study published by Wang et al [51] consisted of 10 studies in a meta-analysis. In addition to the significant effect of music, this study handled the present heterogeneity by conducting a subgroup-analysis, in which the sleep disorders were divided into acute and chronic statuses, that still showed important heterogeneity among studies. The other subgroups of different follow-up durations (<4 days, 4 days to 2 weeks, 3 weeks to 4 weeks) indicated the significant heterogeneity among groups, so did the different measurements of sleep (subjective/objective). Concerning this study, it might be meaningful to point out that the given subgroup-analyses explained somewhat possible sources of heterogeneity between studies. The further expectation is to reduce the present heterogeneity (better $I^2<40\%$ or at least Chi^2-statistic must be not significant). Thus, the evidence for efficacy of music intervention could be more robust.

Compared to the preceding research, Jespersen et al. [52] merged only five studies in a meta-analysis, since the author included music listening as intervention alone and strictly required the inclusion criterion of insomnia in accordance with whether certain documentation was provided. One might concern that the sleep disturbances in ICU/CCU occur very often but not be diagnosed practically. This review study conducted subgroup-analysis for gaining more practical knowledge of music intervention, in which the individual preference of music (chosen from music databank predestined by researchers) exhibited a slight benefit superior to researcher-selected music; yet music listening with or without the relaxation instruction could not influence its efficacy more.

An updated conclusion based on those obvious evidences can be given generally as follows: listening to music can assist patients before bed-time, regulating emotion, mind, and biological mechanism, making the more comfortable surroundings for getting into sleep. Listening to sedative, quiet music styles makes positive progress in sleep quality, enhancing the relaxation, and distracting participants from the main diseases, e.g. pain disorders, anxiety, consequently. Besides, it is believed that the music chosen by participants produces more positive effectiveness. Concerning this, it has to note that the music options were almost pre-selected and pre-recorded by researcher before participant’s selection. The treatment duration of three weeks is proposed currently for obtaining the statistical significance of effectiveness.

1.4 Need of research

Several previous studies were verified that music intervention was an effectual approach for dealing with sleep disorders, especially to improving subjective sleep quality in insomnia. As regards the sleep outcome measurement responding to music effect, most of the studies assembled in previous reviews used insomnia questionnaires, e.g. PSQI, RCQ, for evaluating the sleep quality [50, 52, 53]. The physiological measure, e.g. Polysomnography, was merely applied in a small number of studies. Furthermore, as far as the relevant research is concerned, subjective and objective outcome assessments consist of different dimensions of sleep. Indeed, the physiological measures estimate the biological changes particularly, unlike subjective evaluation, which might be influenced by individual predilection more or less [54]. However, one of the review studies still included sleep efficiency (a kind of PSG's indicators) into the primary meta-analysis [53]. As a result, the rest of PSG indicators were ignored. The other two reviews were not analyzed the PSG outcome data due to the insufficient amount of study [50, 52]. One might assume that the PSG as a dynamic measurement could provide more objective evidences of effectiveness of music for sleep research. PSG could exhibit a portrait of human brain in response to music during sleep.

The other reason for doing this current review is to extend general clinical application of music in various sleep-related problems; meanwhile, to detect more possible influential factors on the implementation of music. For a more reason, many potential studies indexed in Chinese databases may have the certain contribution to this current topic but were neglected by previous researchers, because those studies were written in Chinese wholly or provided only partly English abstracts. They are definitely considered in this research.

2 Aims and objectives

Thanks to the previous studies, they did supply the relevant cues for further explorations. Thus, this current review intends to investigate the present state of clinical music intervention and to explore how music intervention works on the progression of sleep in the different patients with sleep disorders by handling outcome data according to their fitting properties, e.g. sleep questionnaires and polysomnography, respectively. In order to derive more concrete indications concerning practicing music in clinical fields, this systematic review is furthermore aiming to elucidate the effect of music underlying multiple clinical factors through answering the following questions:

(1) How is the general state of using music in various sleep-related problems? (This question may show the concern with what kind of sleep problems has been alleviated by music intervention.)

(2) How could the effectiveness of music interact with the given clinical diversities? (This current review is focused on those factors: increasing age, specified clinical conditions, treatment durations, weekly frequency of using music, and music parameters.)

(3) Could the 'dosage' of music be specified in treating different sleep problems?

3 Methodology

This review was performed according to the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011] [55] and PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) guideline [56]. The relative search method was conducted by two researchers independently, so was the process of study selection undertaken firstly by screening titles and abstracts, secondly by viewing the full texts of potential studies.

3.1 Criteria for considering studies for this review

Only randomized controlled trials were accepted. There was no limitation of publication status, publication year or language.

3.1.1 Types of participants

The potential studies involved various participants with sleep problems. Those sleep problems could be the acute or chronic sleep disturbances; they could also present in company with other primary disorders. For instance, some studies received people being diagnostic of a certain type of sleep disorder; some received people only complained about their difficulty in falling asleep without clear diagnosis (e.g. elderly people).

Given that the clinical conditions corresponding to sleep difficulty are complicated and thus required to be defined clearly, the following two types of participants were basically considered:
(1) Participants had been diagnosed as the ICSD-3 [6] defined insomnia disorder. According to this classification, insomnia disorder was characterized by persistent difficulty initiating sleep or maintaining asleep in spite of the adequate sleep opportunity, and daytime impairments. The related diagnoses could be involved in chronic insomnia, short-term insomnia, or other insomnia disorder.
(2) Participants commonly suffered from sleep disturbance in some medical conditions, such as staying in ICU/CCU, surgery-related status. In such patient groups, the insomnia symptoms might happen predictably, but an insomnia-related diagnosis might be established after discharging the hospital, if the sleep disturbance frequently occurs.

For the purpose of validating the specific effect of music on sleep, there were no restrictions as to age, gender, or ethnicity of participants. People suffering from neurological disorders and complained about sleep difficulty, such as sleep-related epilepsy were also included. As well, the sleep problem in preterm infants was paid attention. (3) Hence, the third type of participants was to focus on other sleep-related problems.

However, people with alcohol or non-prescription drug problems as well as people in persistent vegetative state were excluded.

3.1.2 Types of interventions

The music intervention was not restricted in its performing form (active or receptive), genre, and style. Different kinds of music interventions, such as listening music, playing instruments, music improvisation or singing, were collected. The frequency and length of every treatment were not limited and neither was the music sound volume.

In addition, the music intervention was played alone or combined with a standard treatment. On the contrary, the compared group received non-treatment, or placebo (e.g. music video), or underwent a standard therapy (e.g. cognitive behavior therapy).

Besides, the music relaxation program in a few studies comprised music, muscle relaxation and/or mental imagery. This kind of music relaxation program was counted in one type of music interventions. Concerning this, whether the effectiveness simply comes from music itself may become a matter for argument. However, this music intervention with restricted multi-components was still included, since this current study attended to estimate the general effectiveness of music on sleep disorders; on the other hand, it could not be completely excluded due to insufficient information of eligible studies. For instance, one might specify alone "listening to relaxing music" in the intervention group. In such a study, the instructions of muscle relaxation might be given to participants more or less before or during music listening. Afterward, more details were described in the section "Handling of disagreements".

3.1.3 Types of outcome measures

(1) Primary outcomes

Sleep quality is a general aspect in different cases of sleep disorders, which are traditionally measured either through reliable sleep questionnaires, such as Pittsburgh Sleep Quality Index (PSQI) [57], Verran and Snyder-Halpern (VSH) [58], or through Polysomnography (PSG) and actigraphy [59]. Sleep evaluation scales and diaries belong to subjective evaluation of individuals, which have been proofed in their sensitivity to sleep parameters over time [54]. In comparison with sleep questionnaire, PSG can objectively measure individual's sleep and provide a quantitative evidence for diagnosis. One might think of using sleep questionnaire, that could offer a more natural environment during the assessment of sleep quality. Nevertheless, a multi-method approach for assessing sleep was suggested in a few studies. They reported the largest discrepancies between sleep diary and PSG [60, 61]. For the sake of consolidating primary outcome, the subjective (self-rating) and objective estimates of sleep quality were taken into account.

As mentioned, the sleep questionnaires are used to portray the sleep quality. They consist of several items for measuring the current symptom severity of the participant. In addition, the specific physical estimators, such as sleep-wake schedule or distinct stages of brainwave, could be measured by PSG. The relevant sleep variables showing in this review were descriptive in

Table 1 Definitions of sleep variables and parameters. In healthy adults, approximately 5% of the total sleep time occurs in sleep stage N1; 50% in N2 sleep stage; and 20% in N3 sleep stage. The remaining 25% is REM sleep stage. The average duration of quiet sleep epochs in premature babies (≥32 weeks' gestational age) is 24-28 minutes. For more details, please refer to Olischar et al. [49], Smith and Wegener [54], and Richards [62].

Table 1 Definitions of sleep variables and parameters

Sleep quality: e.g. Pittsburgh Sleep Quality Index (PSQI)	
1) Subjective Sleep Quality; 2) Sleep Latency; 3) Sleep Duration; 4) Habitual Sleep Efficiency; 5) Sleep Disturbance; 6) Use of Sleep Medication; 7) Daytime Dysfunction.	
Sleep quantity: e.g. Polysomnography (PSG)	
1) Total Sleep Time (TST):	Total amount of time spent in bed
2) Sleep Efficiency (SE):	Percentage of total time spent in sleep. It goes throughout 4 stages and REM sleep. The sum of real sleep time is divided by the total time in bed and multiplied by 100.
3) Sleep Onset Latency (SOL):	The length of time from "lights out" to the first sleep stage.
4) Wake after Sleep Onset (WaSO):	Time-span of wakefulness occurring after sleep onset.
5) Sleep stages N1-N3 (NREM):	Stages of non-rapid eye movement are usually calculated in percentage: total length of each sleep stage divided by total sleep time.
6) Sleep stage REM :	Stage of rapid eye movement calculated in percentage. REM sleep cycle every 90 to 120 min.
7) Sleep-wake-cycling:	Achieving by aEEG (Amplitude-integrated electroencephalography). It could be calculated in terms of duration and number of quiet sleep epochs, minimum and maximum amplitudes, as well as length between two quiet sleep epochs in minutes.
8) Seizure rates:	Seizure occurrence in subjects with neurological handicaps, e.g. epilepsy.

(2) Secondary outcomes

Sleep deprivation reflects a potential healthy problem. A certain diagnosis of sleep problem involves mental and physiological observations. Therefore, the secondary outcomes contained the relevant evaluation of emotion (e.g. reducing extreme terror, panic, depression, and anxiety), as well as the evaluation of pains.

3.2 Search methods

The following search term was utilized without restrictions of language or publication status by using title, abstract, keywords and text:

music (music therapy or music intervention or music medicine) AND sleep disorders (sleeping problem OR insomnia OR hypersomnia OR Nightmares OR sleep-wake OR Sleep terror OR sleep apnea OR restless legs syndrome OR Sleepwalking)

Medical Subject Headings (MeSH) and EMTREE were equally used for identifying different search concepts. The databases listed below were searched from the first date available until April 2017,

- Cochrane Central Register of Controlled Trials,
- MEDLINE through PubMed,
- EMBASE through DMDI (Deutsches Institut für Medizinische Dokumentation und Information),
- PsycINFO,
- CINAHL,
- Google scholar
- Web of Science
- China Academic Journals Full-text Database (CJFD)

Web of Science (ISI Web of Knowledge) was explored, which integrates the most significant conference proceeding- Conference Proceedings Citation Index and the other three citation databases: Science Citation Index Expanded (SCI-Expanded), Social Sciences Citation Index (SSCI), Emerging Sources Citation Index as well as Arts & Humanities Citation Index (A&HCI). Besides, Korean Journal Database, Russian Science Citation Index and SciELO Citation Index were also searched through Web of Science.

In China Academic Journals Full-text Database, over thousand China academic journals and full-texts have been collected. The relevant studies are written only in Chinese but with English abstract (Appendix A).

For complete data collection, the ongoing trials were also checked through

- National Research Register,
- ClinicalTrials.gov, and
- Current Controlled Trials.

Furthermore, some representative journals in the research field of music therapy have already been indexed by MEDLINE. They were searched through PubMed.

- Journal of Music Therapy (British Journal of Music Therapy)
- Nordic Journal of Music Therapy,
- Australian Journal of Music Therapy,
- Canadian Journal of Music Therapy, and
- Music Therapy Perspectives.

On the basis of the availability, some of conference proceedings were extra explored as follows:

- Annual Meeting of the Associated Professional Sleep Societies LLC (APSS), 2011-2016
- World Association of Sleep Medicine (WASM), 2015
- International Pediatric Sleep Association (IPSA), 2010
- 12th International Symposium “Sleep and Breathing”, 2011

In the initial searching, 258 studies were found by searching in databases and three studies were collected by searching in 2011 conference proceeding of WASM and in 2010 IPSA.

3.3 Data collection and analysis

3.3.1 Selection of studies

The search results were merged by using reference management software Citavi 5 [63], through which most of the duplicate records were automatically removed. Total 97 studies were collected. Then, titles and Abstracts of the studies were firstly scanned by two reviewers in order to retrieve the potentially relevant and to reject the obviously irrelative reports. Stepwise, a sum of 44 studies showed the potential. Consecutively, two reviewers investigated full-text of 44 remaining studies and assessed their eligibility according to the pre-specified inclusion criteria. The PRISMA flow diagram [64] would show a framework of study selection. See Figure 1 PRISMA flow chart in the section of result.

Two reviewers conducted this process of selecting studies and examining full-text reports, respectively. The first reviewer is a clinical methodological expert. The second reviewer is familiar to clinical music interventions. The decisions of eligible studies were made separately. The different opinions were resolved by discussion.

3.3.2 Handling with disagreements

After examination of full-text of reports, the different evaluations were found in three studies [32, 62, 65]. On the basis of PICO model (Population, Intervention, Comparator, Outcome), these studies were explored again in reviewer´s meeting and discussed as follows:

Field et al. [65] attended to modify the mood of adolescent mothers. The quality/quantity of sleep was not the research object. Music was merely one of many therapeutic elements and not clearly defined in its clinical use. In addition to music, those multiple interventions used in Field’s study involved relaxation therapy, massage therapy, and mother-infant interaction coaching. Thus, this study had a shortage of evidence for effect of music on sleep improvement. It was eventually excluded.

In contrast to Field’s study, Richards’ study [62] was included. The intervention called the music relaxation program consisted of progressive muscle relaxation and mental imagery. One may doubt about its eligibility. As to this argument, it has been given a reasonable explanation though the basic method of music therapy. The Guided Image and Music (GIM) or the Bonny Method, is developed by Helen Lindquist Bonny with a foundation of psychotherapy. It focuses on the spiritual transformations in response to classical music elements. For instance, any of life events could be a therapeutic theme evoked by music and progresses in participant's image [66, 67]. In Richards' study, it did not specify clearly, whether or not the mental imagery was a practice of Bonny Method. However, considering the nature of music and the information offered in the study, this mental imagery should be induced by music and continued during listening music. Therefore, Richards 1998 was included in the review.

Bodner et al. [32] aimed to reduce occurrences of epilepsy through a long-term musical interference. The setting of music intervention was clarified. The argument of this report lay in definition of outcome, whether the reduction of epilepsy related to sleep quality. Indeed, the study indicated a significant result after dealing with music listening, that the events of epilepsy apparently decreased, and furthermore, some of the participants did not experience epilepsy in follow-up phase any more. Indeed, it helped participants to recover a normal sleep pattern-- a sleep-wake cycle. In view of this above point, this study was evaluated to be qualified.

There were no important disagreements to consult with the third reviewer. The kappa statistic was calculated for measuring agreement between two reviewers (Appendix B).

3.3.3 Data update

Searching of potential studies was conducted firstly in 2012 and renewed again in 2016 according to the searching strategy. There were 19 studies found additionally. They were screened in titles and abstracts by the main author alone, so were in full texts as well. Consequently, there were seven studies qualified. Then, the risk of bias was evaluated in the eligible studies. The up-to-date result was documented in the next chapter.

3.3.4 Data extraction and management

The final eligible studies were itemized using the united form of data extraction and tabled afterward in the Appendix C. The data extraction sheet was developed in five dimensions for managing important data. These dimensions contained 1) general information, 2) methods characteristics, 3) trials and participant's characteristics, 4) interventions characteristics, and 5) outcomes. Besides, the excluded studies were given the primary reasons summarized in the Appendix D. The duplicate records were merged into the up-to-date reports.

3.4 Assessment of risk of bias

The quality of randomized controlled trials was inspected by using the Cochrane risk of bias tool [68]. This tool was made up of two parts. One was to describe what happened in the selected trial; the other was to do the judgment of review authors concerning risk of bias in the trials. The former part included six relevant domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias. On the basis of these domains, the latter part of judgment was done via entries of "Yes", "No" or "Unclear". An answer “Yes” indicated a low risk of bias; “No” indicated a high risk; “Unclear” indicated an unclear risk. When insufficient information was commented, it was rated “unclear”. Any discordant opinions were discussed in detail.

More details about assessing risk of bias have been summarized in the Cochrane Handbook for Systematic Reviews of Interventions, section 8.5, where a given criteria tabulation exhibits a quick view for judging risk of bias [69].

3.5 Measures of treatment effect

Firstly, the natures of outcomes data were described. The extracted outcomes data were inputted into Review Manager (RevMan) [70]. The continuous outcome data from different questionnaires and polysomnography were estimated by using mean difference (MD), when the same scale or the same unit of measurement was applied among trials; using standard mean difference (SMD) with 95% CI, when the measure scales varied among the trials. The values from different scales had to be converted, when the direction of evaluation was opposite (Appendix E). Concerning the direction of evaluation in this current study, it was appointed, that the lower score reflected the better quality of sleep. For ordinal outcome data, the corresponding items were merged to be dichotomous outcomes for calculation of effect size, e.g. Self-Rating Anxiety Scale (SAS) was based on a Likert-type scale, where the sleep quality was asked by a question: "I fall asleep easily and get a good night's rest? " with a 4-level answer: 1) most of time; 2) good part of the time; 3) some of the time; 4) a little of the time. In this study, the first and the second options were combined to be a positive response, so were the third and the fourth options but to be a negative response [71].

3.6 Unit of analysis issues

A simple parallel group design occurred in most studies included, where the participants are randomized to one of two intervention groups, and the measure for each outcome was collected and analyzed at one time point. In addition, some clinical designs were also taken into account, such as cross-over trial, trial with three or more treatment groups, trial with outcome measurement at several time points. In this current study, an only cross-over trial was not combined into meta-analysis, because the wash-out time was not defined clearly [72]. In the trials with multi-arm design, the most relevant treatment group (e.g. music) versus placebo/control group (e.g. behavior therapy or standard care) was determined for analysis [40, 41, 73–75]. In the trials with several measuring time points, the outcome data in different time points were documented and compared to each other [76–78].

3.7 Dealing with missing data

It was desired to collect outcomes data completely into the same format, such as the mean value and its standard deviation from each intervention. However, data was not always assembled entirely. About the missing participant due to withdrawal, the drop-out rate was reported, where a 10% drop-out was concerned. Dependent on the type of missing data, there were three ways to deal with. In some cases, to convert available data from the study was the first practical way. For example, when the standard deviation was not provided, it was obtained from its standard error multiplying the square root of the sample size: $SD = SE \times \sqrt{N}$. Likewise, the length of 95% confidence interval, the P-values or T-values are important results to report in general. They could be used to derive the standard error, and then to calculate standard deviation [55].

The second was to view the other relevant review-articles, which had investigated the same missing data by asking the author of the study. After practicing the first and second way, all necessary values were found. Thirdly, to come into contact with the author directly was applied as well, in order to fill insufficient information.

3.8 Assessment of heterogeneity

In RevMan, the result of using the chi-squared test (Chi^2, or X^2) for assessing heterogeneity to obtain the Q statistic and its P-value showed in the forest plot. Important was to consider that most of the studies had small sample size or were few in number. In this situation, the chi-squared test had merely a low power. That means, it could still contain a problem of heterogeneity in spite of the non-significance showing in Q statistic. Therefore, a P value smaller than 0.10 instead of 0.05 was picked up for determining the statistical significance of heterogeneity. Further, the value of I^2 was also calculated for the degree of variability in total effect estimates, which indicated how the heterogeneity among studies has an impact on the result of meta-analysis rather than chance. Its equation is: $I^2 = [(Q - df) / Q] \times 100\%$. Higgins et. al. [79] suggested a fundamental understanding of I^2 value: 0 to 40% heterogeneity might not be important; 30% to 60% may present moderate heterogeneity; 50% to 90% substantial heterogeneity; 75% to 100% considerable heterogeneity . However, to interpret the value of I^2 needs a multidimensional observation on effect size, direction of effect, overlap of confidence interval, and strength of evidence.

3.9 Data synthesis

After evaluation of heterogeneity, meta-analysis was undertaken. Although a fixed effects model was chosen in which a low heterogeneity ($I^2 < 40\%$) among studies presented, the random effect model was principally applied for all datasets, so that the result could be seriously interpreted. The pooled WMD or SMD was calculated with 95% CI. Besides, some outcome data that were not available or compatible for merging into a meta-analysis were finally summarized in details.

3.10 Meta-regression and Subgroup-analysis

Diversities come always into existence among studies, owing to different characteristics of population, interventions, study designs, risk of bias. Hence, both meta-regression and subgroup-analysis were undertaken for expanding the explanation about heterogeneity. Meta-regression is usually suggested, when there are more than 10 studies in a meta-analysis in order to ensure the statistical power. [80]. It was performed in a particular package "metafor" through R, in which the meta-regression model was combined with one or more variables (moderators) by using mixed-effects model. Furthermore, this regression model was fitted by the different estimators, e.g. DerSimonian-Laird estimator [81], Restricted maximum-likelihood estimator [82]. Thus, the fitted model could be able to account for the residual heterogeneity among the true effects and then could be used for predicting/simulating the possible true effect.

Concerning subgroup-analysis, as mentioned in the section types of participants, grouping of studies was principally conducted according to whether a certain diagnosis of sleep disorder was made or whether the relevant information of clinical conditions was provided.

3.11 Assessment of reporting biases

The reporting biases refer to e.g. publication, location, citation. Sometimes, the research cannot be published due to a lack of significant result or opposition to the sponsor. As to detecting reporting biases, a funnel plot of sleep quality assessed by sleep-related questionnaires was performed and observed visually, whether or not the funnel plot scattered symmetrically. For strengthening the reliability of the result, Begg and Egger's tests were conducted in R through a particular meta-analytic package "metafor". They were recommended for estimating asymmetry of funnel plot; especially Egger's test [83, 84]. A p value of less than 0.05 was regarded as statistically significant. If appropriate, we attempted to calculate the impact of important modifier using mixed-effects meta-regression model [85–87] and then examined the asymmetry of the adapted funnel plot. The trim-and-fill method [88] was also used to calculate the number of missing studies and to adjust the effect size.

3.12 Sensitivity analysis

In order to avoid some arbitrary and unclear decisions during conducting the systematic review, a sensitivity analysis was undertaken.

3.13 GRADE approach

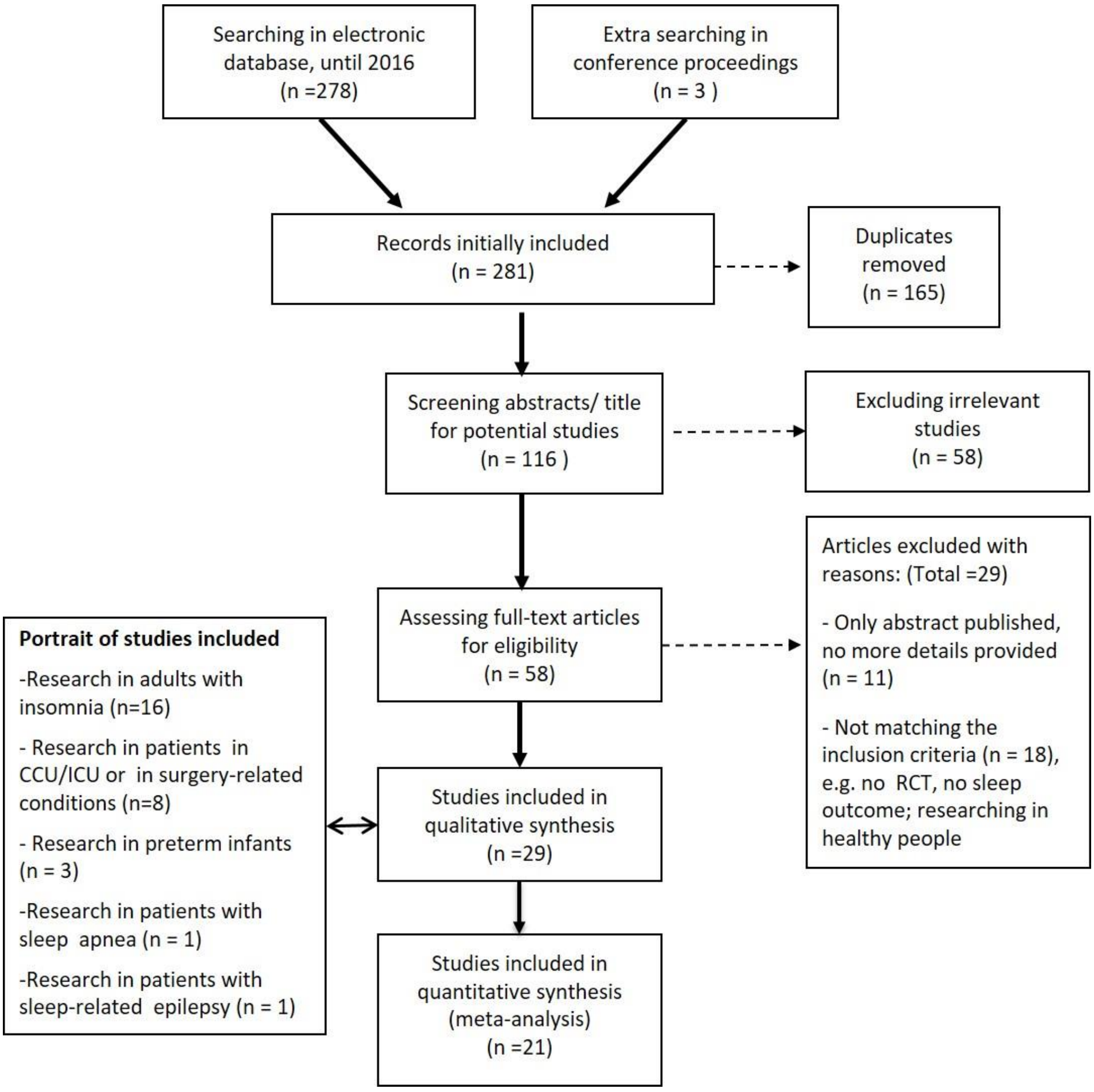
Finally, the evidences were summarized in the GREAD finding table and evaluated again carefully in five dimensions: the items of risk of bias, publication bias, inconsistency, indirectness, and imprecision [89]. These dimensions were integrated in the Guideline Development Tool (GDT) "Das tool" (www.guidelinedevelopment.org).

4 Results

4.1 Description of studies included

There were 29 studies qualified, of which 21 were merged in a meta-analysis; the remaining studies were discussed in details afterward. The procedure of searching method was displayed in the PRISMA flow chart (Figure 1).

Figure 1 PRISMA flow chart



Furthermore, the kappa statistic was calculated. The studies were screened and evaluated by two researchers in the beginning of 2014. It showed 0.94 reflecting an excellent agreement between two researchers (Appendix B). There were seven studies included after 2014 until the end of 2016. The relevant evaluation of studies was conducted by the author alone.

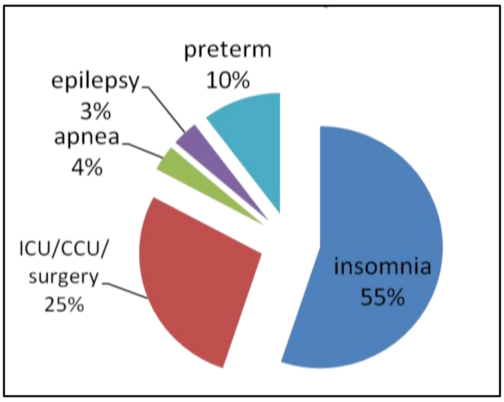
The characteristics of the studies were basically summarized in Table 2 including study information (authors, year of publications), participant information (age, clinical conditions, nation), music intervention (duration of treatment, frequency of usage), control groups, and sleep-related outcome assessments. Listening to music was mostly chosen in the studies. Only one study explored the benefit of didgeridoo playing to patients with sleep apnea. More details were attached in Appendix C. The status of music intervention in the current sleep research was drawn in a pie chart labeled with percentage, respectively (Figure 2).

Table 2 Basic characteristics of studies

Study	Year	Average age	Patient groups (Conditions)	Duration	Nation	Control group	Frequency	Sleep outcomes
Bodner	2012	36.11	Sleep related epilepsy	1 year (follow up: 1 year)	America	Medication	1 per day	Seizure frequency
Chan	2010	75	Insomnia_elderly	3 weeks	China	No treatment	1 per week	PSQI
Chang	2012	31.82	Insomnia	4 days	China	No treatment	1 per day	PSG
Deshmukh	2009	33	Insomnia_depression	4 weeks	India	Medication	1 per day	PSQI
Harmat	2008	22.60	Insomnia	3 weeks	Hungary	No treatment	1 per day	PSQI
Hu	2015	56.71	ICU/CCU/ surgery	2 days	China	Standard care	1 per day	RCSQ
Kong	2005	38.63	Insomnia disorders	2 weeks	China	No treatment	5 per week	PSQI
Kullich	2003	48.37	Insomnia_pain	3 weeks	Salzburg	No treatment	1 per day	PSQI
Lafci	2015	46.42	Insomnia_cancer	7 days	Turkey	Standard care	1 per day	RCSQ
Lai	2006	67	Insomnia_elderly	3 weeks	Taiwan	No treatment	1 per week	PSQI
Lee	2015	40	Insomnia_cancer	2 weeks	South Korea	Standard care	2 per week	VSH
Liu	2016	N/A	Insomnia_pregnancy	2 weeks	Taiwan	Standard care	1 per day	PSQI
Ma	2004	39.50	ICU/CCU/ surgery	1 night	China	Standard care	1 per night	SAS
Mottaghi	2015	68.08	Insomnia_elderly	4 weeks (follow up: 3 months)	Iran	No treatment	2 per day	PSQI
Neal	2008	33.5 gestation	Preterm baby	N/A	America	Ambient noise	N/A	Infant behavioural state
Neander	2004	71.74	ICU/CCU/ surgery	7 days	Germany	Standard care	2 per day	EEG
Olischar	2011	35.9 gestation	Preterm baby	1 night	Austria	Standard care	1 per night	EEG
Puhan	2006	20.68	Sleep apnea	4 months	Zurich	No treatment	5 per week	ESS
Reinhardt	1999	55	Insomnia_cancer	13 days	Germany	Standard care	1 per day	Percentage of falling asleep
Renzi	2000	46	ICU/CCU/ surgery	1 night	Italy	Standard care	1 per night	VAS
Richards	1998	65.8	ICU/CCU/ surgery	1 night	Ameria	Standard care	1 per night	PSG
Ryu	2012	61.2	ICU/CCU/ surgery	1 night	South Korea	Standard care	1 per night	VSH / length of sleep
Schlez	2011	32 gestation	Preterm baby	1 night	Israel	Kangraroo care	1 per night	Infant behavioural state
Shum	2014	64.0	Insomnia_elderly	6 weeks	Singapore	No treatment	1 per day	PSQI
Su	2013	61.68	ICU/CCU/ surgery	1 night	Taiwan	Standard care	1 per night	VSH / PSG
Suwansathit	2015	53.25	Insomnia	1 night	Tailand	Standard care	1 per night	PSG
Wang	2016	69.38	Insomnia_elderly	3 months	China	No treatment	1 per day	PSQI
Wepner	2008	47.06	Insomnia pain	4 weeks	Austria	Standard care	1 per day	ECG (PSG)
Zimmerman	1996	67	ICU/CCU/ surgery	3 days	America	Standard care	1 per day	RSQ

N/A: not available

Figure 2 Music using in different patient groups with sleep problems

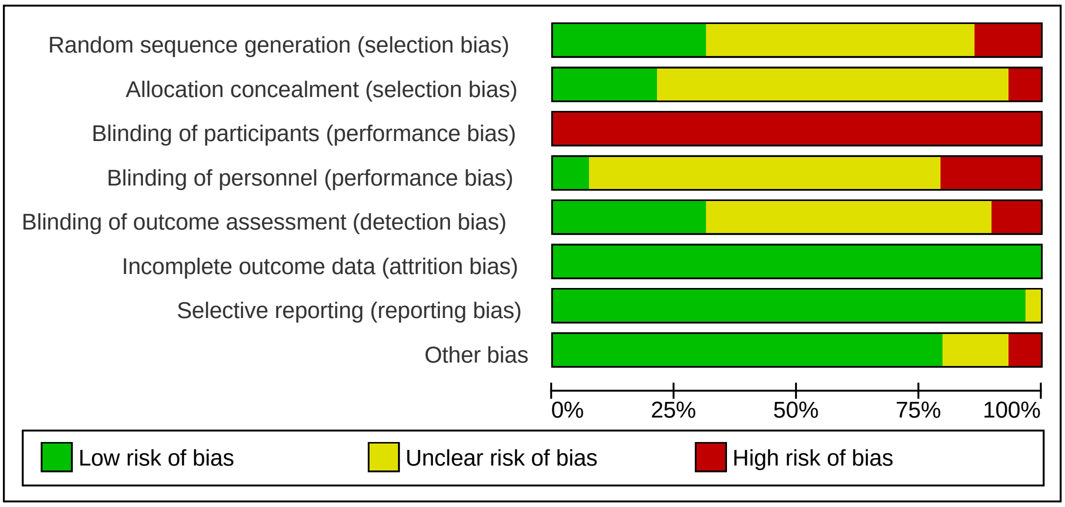


All sleep-related records in the past twenty years (1998-2017) were searched. Only randomized control studies were included.

4.1.1 Risk of bias

The quality of the studies was assessed through the Cochrane risk of bias tool [68] (Figure 3 and Figure 4 on the next page)**.** These two figures indicated the shortage of blinding of participants in all of the studies. The blinding of personnel (about 10% of the whole study) and the blinding of outcome assessor (about 30%) were only done in the small number of study. Likewise, random sequence generation was obtained in approximately 35% of the total number of study; so was allocation concealment achieved in nearly 20% of the total number of study. Though the items of incomplete outcome data, selective reporting, and other bias were controlled in over 75% of the whole study, the remaining items were evaluated mostly as unclear risk of bias, due to the insufficient information in the original reports.

Figure 3 Risk of bias graph



4.2 An overview of analysis methods

21 studies were included in the upcoming meta-analysis. The data types were initially concerned. By using RevMan 5.3, the important values estimated from various sleep-related assessments were keyed in with a united form of mean and standard deviation. Some values from scale-basic assessments, e.g. RCSQ, had to be converted in the inverse direction, so that the evaluation of data could have a consistent definition; that is the smaller value means the better sleep quality. Some of the studies reported the results only in mean and standard error, which was recalculated to its standard deviation by the author as well (Appendix D).

Furthermore, the entire data was handled independently in two types of continuous data: sleep questionnaire and polysomnography (PSG). The relevant analyses consisting of heterogeneity test, meta-regression, subgroup-analysis, and sensitive-analysis for testing within- and between-group diversities were exhibited in the following sections. By using meta-regression, the potential effect of modifiers across studies could be counted in. It could offer a clue for subgroup-analysis. The effect sizes of the studies in the subgroups were united on the basis of random- or fixed effects model. Besides, some studies were excluded from meta-analysis due to incompatible outcome data. Nevertheless, those studies could be crucial to hint more possible techniques of music intervention and to trigger researcher's attention to other sleep-related subjects. Seeing this, the studies apart from meta-analysis were delineated as well.

Figure 4 Risk of bias summary

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants (performance bias)	Blinding of personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bodner 2012	+	?	−	−	+	+	+	+
Chan 2010	+	?	−	−	−	+	+	+
Chang 2012	?	+	−	?	+	+	+	+
Deshmukh 2009	?	?	−	+	+	+	+	+
Harmat 2008	+	?	−	?	?	+	?	+
Hu 2015	+	?	−	?	?	+	+	+
Kong 2006	?	?	−	?	?	+	+	+
Kullich 2003	?	?	−	?	?	+	+	+
Lafci 2015	+	+	−	−	?	+	+	+
Lai 2006	−	+	−	−	−	+	+	+
Lee 2015	?	?	−	?	?	+	+	?
Liu 2016	?	?	−	?	?	+	+	?
Ma 2004	−	?	−	?	?	+	+	?
Mottaghi 2015	?	?	−	?	?	+	+	+
Neal 2008	+	?	−	?	+	+	+	+
Neander 2004	?	?	−	?	?	+	+	+
Olischar 2011	+	+	−	?	+	+	+	−
Puhan 2006	?	+	−	?	+	+	+	+
Reinhardt 1999	−	?	−	?	?	+	+	+
Renzi 2000	+	+	−	?	−	+	+	−
Richards 1998	?	?	−	+	+	+	+	+
Ryu 2011	−	−	−	?	?	+	+	+
Schlez 2011	?	?	−	?	+	+	+	+
Shum 2014	+	−	−	−	?	+	+	+
Su 2013	?	?	−	?	+	+	+	+
Suwansathit 2015	?	?	−	?	?	+	+	?
Wang 2016	?	?	−	?	?	+	+	+
Wepner 2008	?	?	−	−	?	+	+	+
Zimmerman 1996	?	?	−	?	?	+	+	+

4.3 Meta-regression (Moderator-analysis)

Suppose conducting a moderator-analysis could give more explanatory variables for detecting what the heterogeneity could be attributed to. Under the moderator-analysis, a meta-regression was performed in R with a particular meta-analytic package "metafor". According to the compatibility of existing datasets, meta-regression was modeled on the basis of seventeen studies. Those studies contained principally the continuous type of outcome data assessed by various questionnaires of sleep quality. After merging of effect sizes with random-effect model, the substantial heterogeneity was present ($I^2 = 91.75\%$, $P < 0.0001$). The following moderators (also called factors or potential effect modifiers) were separately examined with the mixed-effects model: average age, patient groups (clinical conditions), duration of treatment, and frequency of using music. The results of meta-regression reflected the degree of residual heterogeneity (QE) as well as the significance of moderators (coefficients, QM). The moderator test identified that the factor of specified clinical conditions was the most important variable to influence the effect (QE= 16.84, P = 0.1557; QM = 163.7378, P < .0001), especially insomnia in cancer patients (Table 3). Though the factors of average-age showed significance as well (QM = 14.6675, P = 0.0007), the substantial heterogeneity (here the residual heterogeneity/unaccounted variability was calculated) still remained among the studies (QE = 179.0222, P < .0001). Moreover, the statistical significance of moderator test did not indicate a linear relationship between the treatment effect and the factor duration of treatment (QM = 4.9078, P = 0.2969), as well as frequency of using music (QM = 0.0130, P = 0.9092).

Table 3 Clinical conditions of participants showing in a moderator-analysis

Test for Residual Heterogeneity: QE(df = 12) = 16.8398, p-val = 0.1557							
Test of Moderators (coefficient(s) 2,3,4,5): QM(df = 4) = 163.7378, p-val < .0001							
Model Results:							
	estimate	se	z-val	p-val	ci.lb	ci.ub	
Intrcpt (icu/ccu)	-1.2201	0.2154	-5.6632	<.0001	-1.6424	-0.7978	***
Insom_cancer	-6.2444	0.5753	-10.8533	<.0001	-7.3720	-5.1167	***
Insom_chro	0.6661	0.3148	2.1158	0.0344	0.0491	1.2831	*
Insom_unsp	0.5491	0.2398	2.2894	0.0221	0.0790	1.0192	*
surgery	0.6960	0.2973	2.3414	0.0192	0.1134	1.2786	*

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

4.4 Subgroup-analysis

4.4.1 Establishment of study groups

According to the differential patient conditions, total 2013 participants were initially grouped into the following types (Table 4):

Table 4 Sample sizes in different patient groups

Groups	N. studies*	Sample Size
Insomnia	16	1116
ICU/CCU/surgery	8	723
Sleep apnea	1	25
Sleep-related epilepsy	1	25
Preterm infants	3	113
sum	29	2013

*N.studies: number of studies

(1) Insomnia: Studies, in which the participants were defined as insomnia disorder using certain diagnostic criterion, e.g. PSQI>5 on baseline, with the portrait of general insomnia symptoms (persistent sleep difficulty, despite adequate sleep opportunity, and associated daytime dysfunction).

(2) Sleep disturbances: Studies, in which sleep problems could be predictable in the following clinical conditions: surgery-related treatment, staying in CCU/ICU. In those studies, the acquired sleep problems might continue in some individuals after hospital discharge. Thus, a pre-diagnosis of insomnia might be impossible.

(3) Other sleep problems: Studies, in which the participants suffered from sleep disorders other than insomnia, such as sleep-related breathing problem, sleep-related epilepsy. It must be noted that those sleep disorders mostly have basic symptoms like insomnia. Besides, this section was also involved with the sleep development in NICU that aimed to assist preterm infants in obtaining a regular pattern of sleeping and waking.

Treatment duration of studies lasted from one day to six weeks; two studies followed up to three months [51, 75]; one epileptic study used music for one year [32]. Most of the included studies (85%) were conducted by parallel experimental designs. They selected music listening as a main intervention compared with standard care or placebo group. Three studies were arranged in the form of three-arm trial. One study of preterm infant was carried out by crossover design. Besides, music was played in a few studies (15%) with relaxation techniques. As mentioned in methods, music intervention was only allowed to contain the ancillary instructions of relaxation or "guided imagery" techniques.

4.4.2 Insomnia

16 studies (N = 1116) were categorized in the groups of patients with insomnia; twelve of them were measured by sleep questionnaires, such as PSQI, RCSQ, VRS; three of them were estimated by PSG; one study was apart from meta-analysis due to the incompatible outcome data, but described in details afterward. Table 5 showed 16 studies distributed according the detailed clinical conditions, including chronic illness I (main disorder was depression or pain disorder), chronic illness II (main disorder is cancer), as well as other types (unspecified). With regard to the condition of other types (unspecified), the causation of insomnia was not defined clearly or could not be accounted for, including insomnious elderly people, insomnious adults without specified medical conditions, and pregnant women.

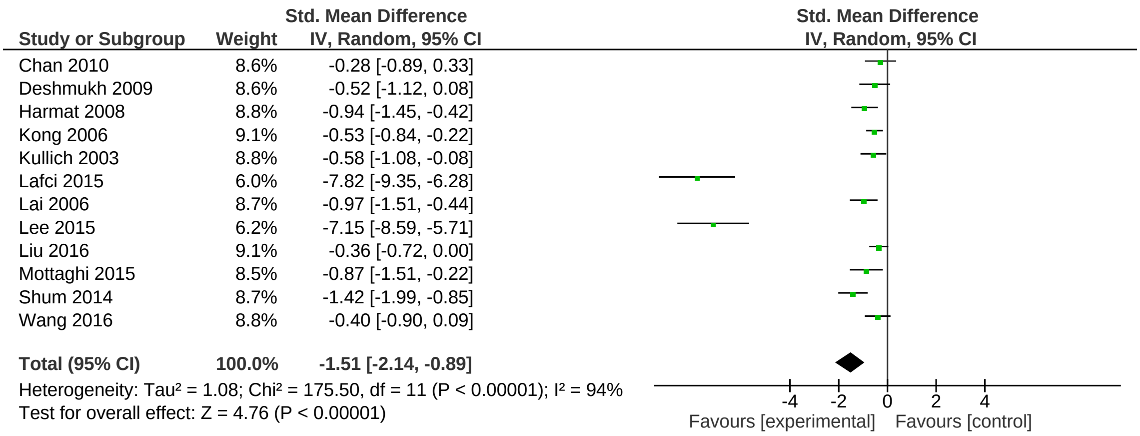
Table 5 Groups of patients with insomnia

Insomnia (Total sample=1116, N. studies=16)				
Outcome measures	Questionnaire		PSG/others	
Subgroups	Numbers	%	Numbers	%
Chronic illness (I)*	2	13%	1	6.3%
Chronic illness (II)*	2	13%	1	6.3%
Others (unspecified)*	8	50%	2	12.5%
Sum	12	75%	4	25%

(1) Outcome data from sleep questionnaires

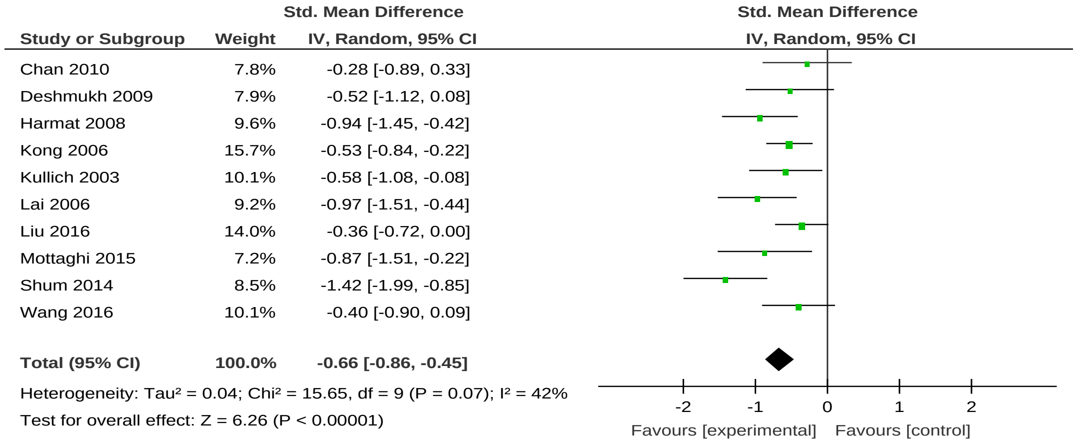
12 studies measured by different sleep questionnaires were merged by using standard mean difference (SMD) as effect size (Figure 5).

Figure 5 Forest plot of insomnia (N = 12)



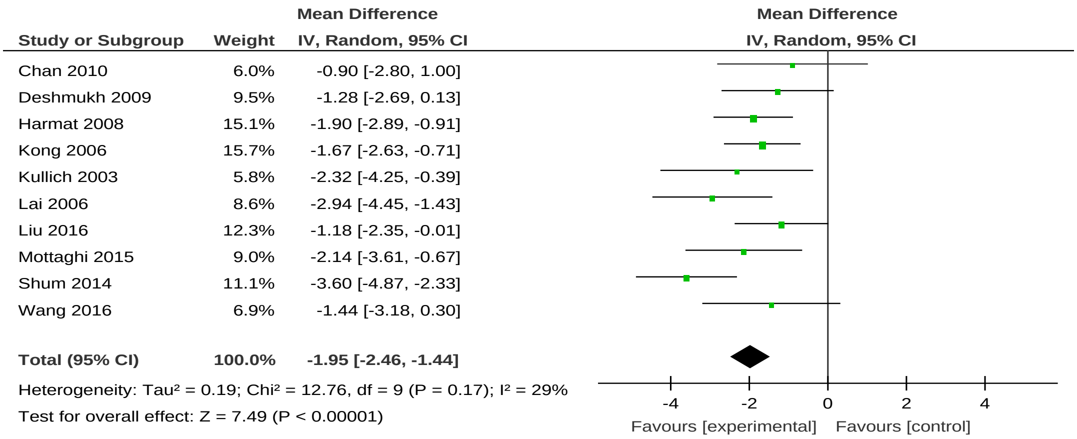
The heterogeneity test indicated a considerable heterogeneity among the studies. ($Tau^2 = 1.08$, $Chi^2 = 175.50$, $P < 0.00001$, $I^2 = 94\%$). This figure showed that two studies in treating cancer patients' insomnia obtained extremely better effects than other studies; thus the heterogeneity was estimated as high [78, 90]. They were independently analyzed in a subgroup analysis afterward. By separating these two studies, the remaining ten studies were combined again. The heterogeneity became moderate (P = 0.07, I^2 = 42%). The overall effect remained as significant (P < 0.00001, SMD = -0.66, CI95% = -0.86, -0.45) (Figure 6).

Figure 6 Forest plot of insomnia (N= 10)



Considering the same sleep assessment PSQI employed in these ten studies, mean difference (MD) was also used to detect the absolute difference among the given 10 studies. As a result, the heterogeneity was decreased again and became not important (Tau^2 = 0.19, Chi^2 = 12.75, p = 0.17, I^2 = 29%). The absolute reduction by using PSQI was pointed on 1.95 points (P < 0.00001, MD = -1.95, CI95% = -2.46, -1.44) (Figure 7).

Figure 7 Forest plot of insomnia with mean difference



Furthermore, subgroup-analysis was conducted. The following subgroups were categorized according to clinical conditions concerning whether the insomniac problems were associated with other specified clinical diseases, such as cancer, pain disorder, depression (Table 5). Several forest plots of subgroups were displayed as follows. Besides, insomnious elderly people (age > 60 years) were also combined in a subgroup (Figure 8, Figure 9, Figure 10, Figure 11).

Figure 8 Forest plot of insomnia in patients with chronic diseases I

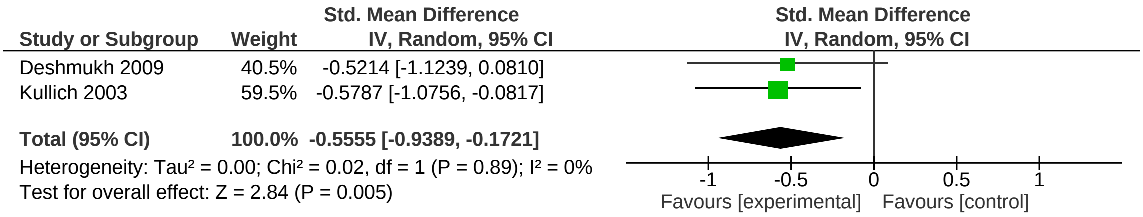
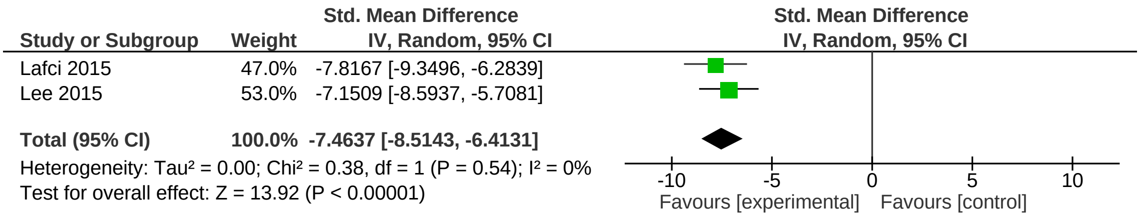


Figure 9 Forest plot of insomnia in patients with chronic diseases II (cancer)



In Figure 10, all of the studies measured sleep quality in insomnia (unspecified) with the same questionnaire (PSQI). By using SMD as effect estimator, the heterogeneity showed a significance (P = 0.03, I^2 = 54%). Otherwise, using MD as effect estimator made heterogeneity to be acceptable (P = 0.11, I^2 = 40%) and then resulted in reducing two points on PSQI (P < 0.00001, CI95% = -2.60, -1.40). With the same consideration, the heterogeneity among studies relating to insomnious elderly people was found with P-value of 0.04 (I^2 = 59%) by using SMD. However, it was then slightly reduced by using MD (P = 0.10, I^2 = 48%) in Figure 11; and the effect size was obtained as 1.92 fewer points on PSQI (P = 0.0001, CI95% = -2.90, -0.93).

Figure 10 Forest plot of unspecified insomnia in adults

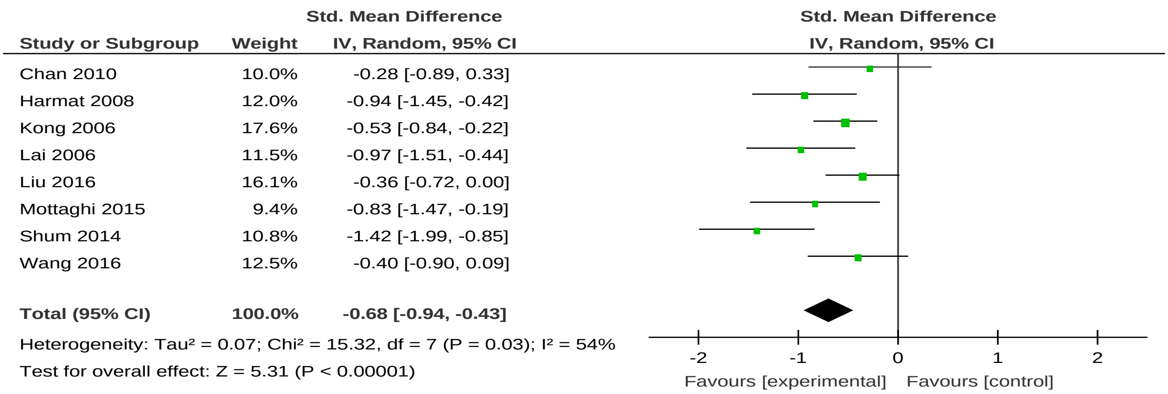
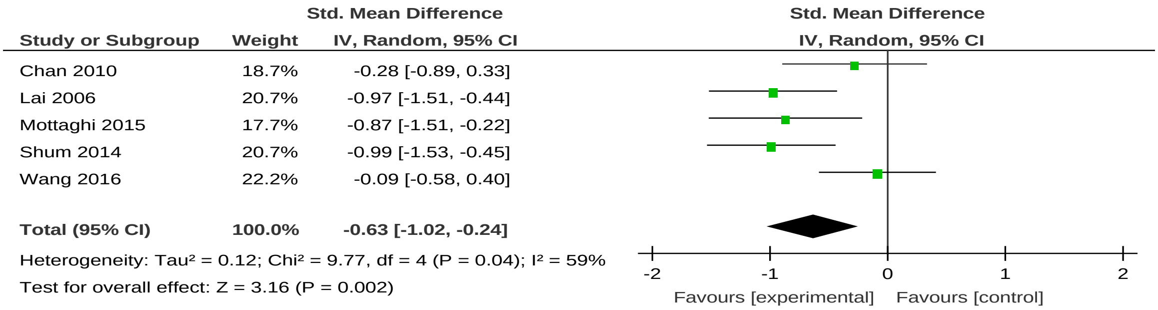


Figure 11 Forest plot of unspecified insomnia in elderly people with treatment 3-4 weeks



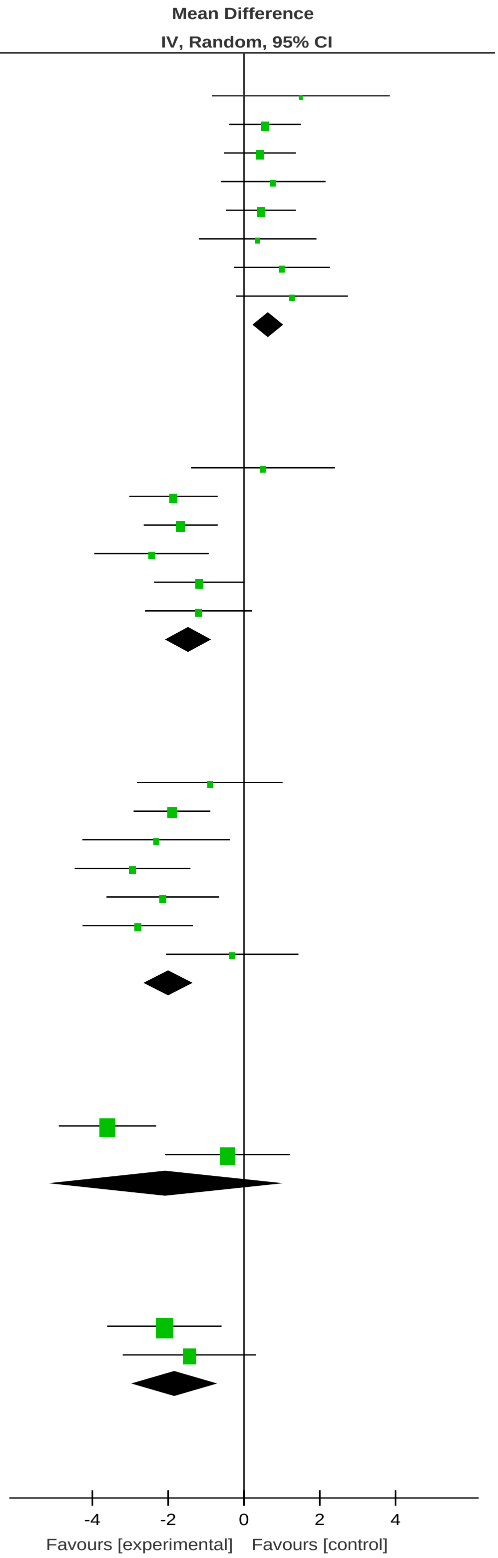
It was especially interesting to investigate the effects in different time-points. Accordingly, it was considered to remove two cancer studies and two studies with specified medical conditions (chronic illnesses: depression and pain disorder), because they may cause some unexpected diversities. Afterward, the eight studies defined as insomnia (unspecified) were assembled into 14 days, 21-30 days, between 1 to 2 months, and over 3 months (Figure 12).

The pre-test of the studies was added to the baseline as well. Hence, a clearer view of change in mean responding to the effect of music intervention was manifested. Due to the use of the same sleep assessments (PSQI) and the similar study designs as well as the lower heterogeneity, mean difference with random-effects model was chosen for merging data.

The heterogeneity was not important in 14 days ($P = 0.16$, $I^2 = 27\%$) and in 21 -30 days ($P = 0.18$, $I^2 = 23\%$). The overall effects presented significance ($P < 0.00001$) in 14 days (MD = -1.45, 95%CI = -2.06, -0.84), in 21 days (MD = -1.98, 95%CI = -2.63, - 1.33). Between 1-2 months ($P = 0.09$, $I^2 = 89\%$), a considerable heterogeneity was detected. It could be caused by different manipulations of music intervention and a small number of studies. Whereas the heterogeneity was estimated as zero ($P = 0.57$, $I^2 = 0\%$) at the time-point of three months, in which the effect achieved a reduction of 1.82 ($P = 0.002$, MD = -1.82, 95%CI = -2.95, -0.69).

Figure 12 Forest plot of unspecified insomnia measured in different time-points

Study or Subgroup	Weight	Mean Difference IV, Random, 95% CI
1.6.1 Insomnia_Sleep quality at baseline (Pre-test)		
Chan 2010	3.2%	1.50 [-0.83, 3.83]
Harmat 2008	20.0%	0.56 [-0.37, 1.49]
Kong 2006	19.8%	0.42 [-0.51, 1.35]
Lai 2006	9.2%	0.77 [-0.59, 2.13]
Liu 2016	21.2%	0.45 [-0.45, 1.35]
Mottaghi 2015	7.3%	0.36 [-1.17, 1.89]
Shum 2014	11.1%	1.00 [-0.24, 2.24]
Wang 2016	8.1%	1.27 [-0.18, 2.72]
Subtotal (95% CI)	**100.0%**	**0.65 [0.24, 1.06]**
Heterogeneity: Tau² = 0.00; Chi² = 2.14, df = 7 (P = 0.95); I² = 0%		
Test for overall effect: Z = 3.07 (P = 0.002)		
1.6.3 Insomnia_Sleep quality in 14 days		
Chan 2010	9.0%	0.50 [-1.38, 2.38]
Harmat 2008	19.5%	-1.86 [-3.01, -0.71]
Kong 2006	24.7%	-1.67 [-2.63, -0.71]
Lai 2006	13.2%	-2.44 [-3.93, -0.95]
Liu 2016	18.9%	-1.18 [-2.35, -0.01]
Shum 2014	14.7%	-1.20 [-2.59, 0.19]
Subtotal (95% CI)	**100.0%**	**-1.45 [-2.06, -0.84]**
Heterogeneity: Tau² = 0.16; Chi² = 6.84, df = 5 (P = 0.23); I² = 27%		
Test for overall effect: Z = 4.66 (P < 0.00001)		
1.6.4 Insomnia_Sleep quality in 21-30 days		
Chan 2010	9.8%	-0.90 [-2.80, 1.00]
Harmat 2008	25.1%	-1.90 [-2.89, -0.91]
Kullich 2003	9.5%	-2.32 [-4.25, -0.39]
Lai 2006	14.2%	-2.94 [-4.45, -1.43]
Mottaghi 2015	14.8%	-2.14 [-3.61, -0.67]
Shum 2014	15.2%	-2.80 [-4.24, -1.36]
Wang 2016	11.4%	-0.31 [-2.04, 1.42]
Subtotal (95% CI)	**100.0%**	**-1.98 [-2.63, -1.33]**
Heterogeneity: Tau² = 0.18; Chi² = 7.84, df = 6 (P = 0.25); I² = 23%		
Test for overall effect: Z = 6.00 (P < 0.00001)		
1.6.6 Insomnia_Sleep quality in 1-2 month		
Shum 2014	51.4%	-3.60 [-4.87, -2.33]
Wang 2016	48.6%	-0.44 [-2.07, 1.19]
Subtotal (95% CI)	**100.0%**	**-2.06 [-5.16, 1.03]**
Heterogeneity: Tau² = 4.44; Chi² = 9.03, df = 1 (P = 0.003); I² = 89%		
Test for overall effect: Z = 1.31 (P = 0.19)		
1.6.7 Insomnia_Sleep quality in 3 months (Follow-up)		
Mottaghi 2015	57.7%	-2.10 [-3.59, -0.61]
Wang 2016	42.3%	-1.44 [-3.18, 0.30]
Subtotal (95% CI)	**100.0%**	**-1.82 [-2.95, -0.69]**
Heterogeneity: Tau² = 0.00; Chi² = 0.32, df = 1 (P = 0.57); I² = 0%		
Test for overall effect: Z = 3.15 (P = 0.002)		

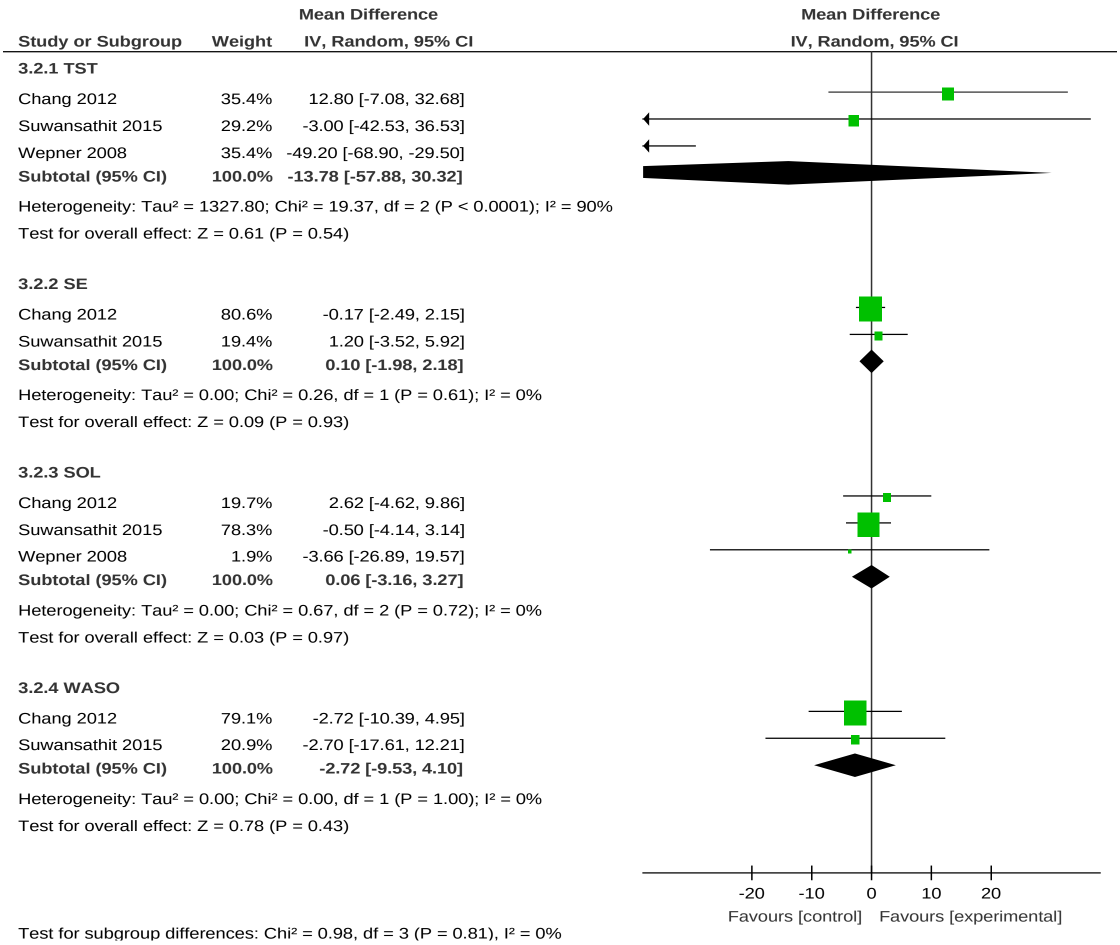


Test for subgroup differences: Chi² = 65.12, df = 4 (P < 0.00001), I² = 93.9%

(2) Outcome data from PSG

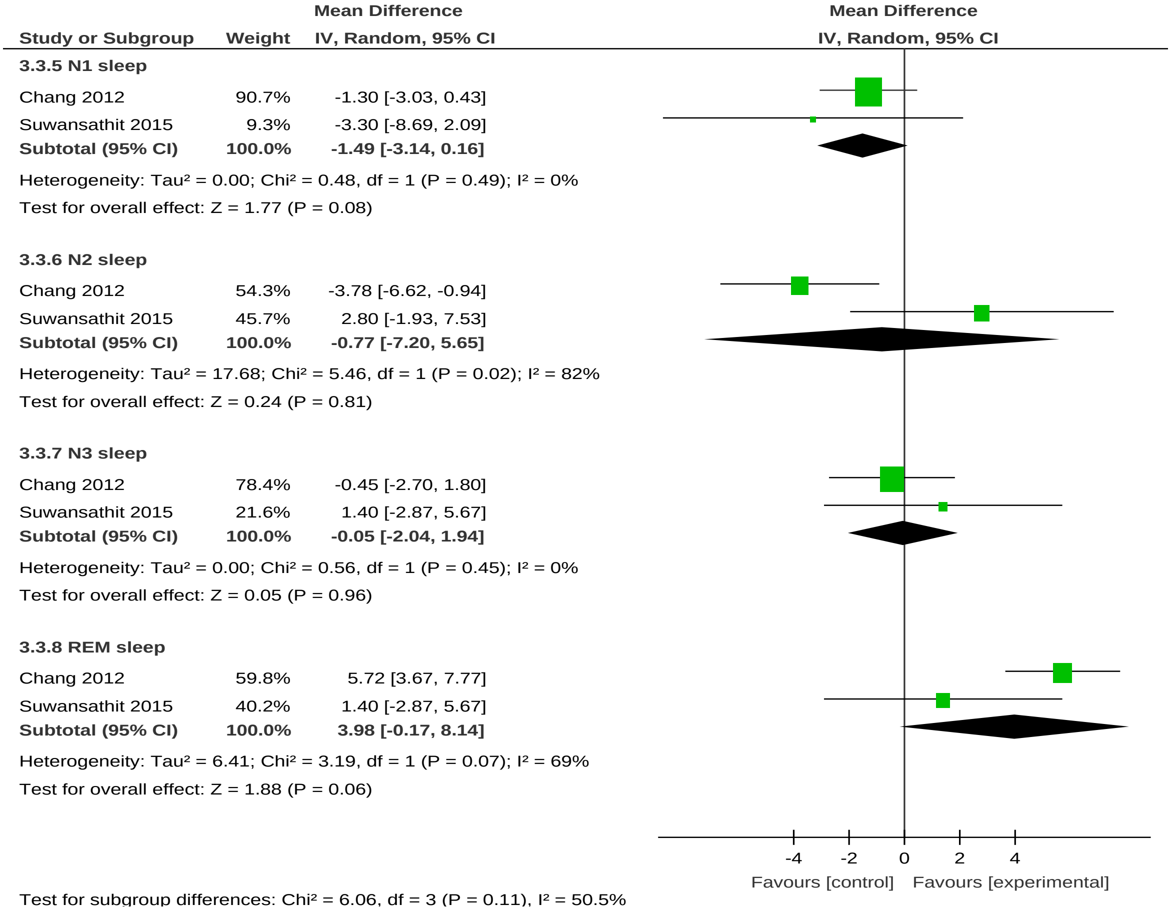
Three studies were considered in the following analyses. PSG consists of several measuring parameters, including TST, SE, SOL, WASO, N1-N3 sleep stages, REM sleep stage. All of them were showed in the sequential Figure 13. The effect estimator of MD with random effects model was concerned, due to the same unit of measure (minutes). The other reason given was that the sleep architecture (sleep N1-N3 and REM stage) was delineated as the percentage of sleep time spent in different sleep stages. Thus, to know, whether the sleep time increased or decreased might help interpreting the effect of intervention.

Figure 13 Forest plot of sleep quantity measured by PSG



The group of TST indicated the substantial heterogeneity (P < 0.0001, I² = 90%). It was concerned, Wepner's study might cause the substantial heterogeneity [41], in which the insomnious patients were mainly associated with low back pain and were treated by a special receptive music intervention, singing bowl. In accordance with the previous definition of insomnia subgroups, this study could be separated in an individual subgroup of chronic disease I (chronic pain) and then the remaining studies could exactly be labeled as unspecified insomnia. Thus, the heterogeneity was minimized very much (P = 0.48, I² = 0%). The studies included in TST were also concerned in the group of SOL, nevertheless, the heterogeneity was not significant. Furthermore, the heterogeneity existing in N2 sleep and REM sleep could not be explained as much. The overall effect in stages of N1 sleep (P = 0.08, MD = -1.49, 95%CI = -3.14, 0.14) and REM sleep (P = 0.06, MD = 3.98, 95%CI = -0.17, 8.14) showed the tendency toward a significant change.

Figure 13 (continue)



(3) Study apart from meta-analysis

Reinhardt [44] conducted a randomized pilot study with 28 cancer patients (age= 44-74 years), using a 30-minute lullaby-like music in the intervention group for 14 days, and recording the synchronization of heart rate with musical beat (48-42 beats per minute) on day 1 and day 15. The intervention group showed the higher degree of synchronization and became more relaxing than the control group. This relaxation shortened the time of falling asleep and decreased the pain intensity resulting in less consumption of analgesics.

4.4.3 Sleep disturbances in ICU/CCU/surgery-related conditions

Eight studies (n= 723) were categorized in the group of sleep disturbances; five of them were measured by sleep questioners, such as VAS, VRS [1, 40, 91–93]; two of them provided the data of PSG [73, 93], in which one study comprised the results of PSG and sleep questionnaire simultaneously [93]. The other two studies were excluded from meta-analysis, due to incompatible outcome data [71, 94]. The patient population was in the age ranging from 40 to 72 years. The general treatment lasted one to three days; only one study was measured after the treatment of seven days [94]. The clinical conditions were specified as staying in ICU/CCU or surgery-related treatment (Table 6).

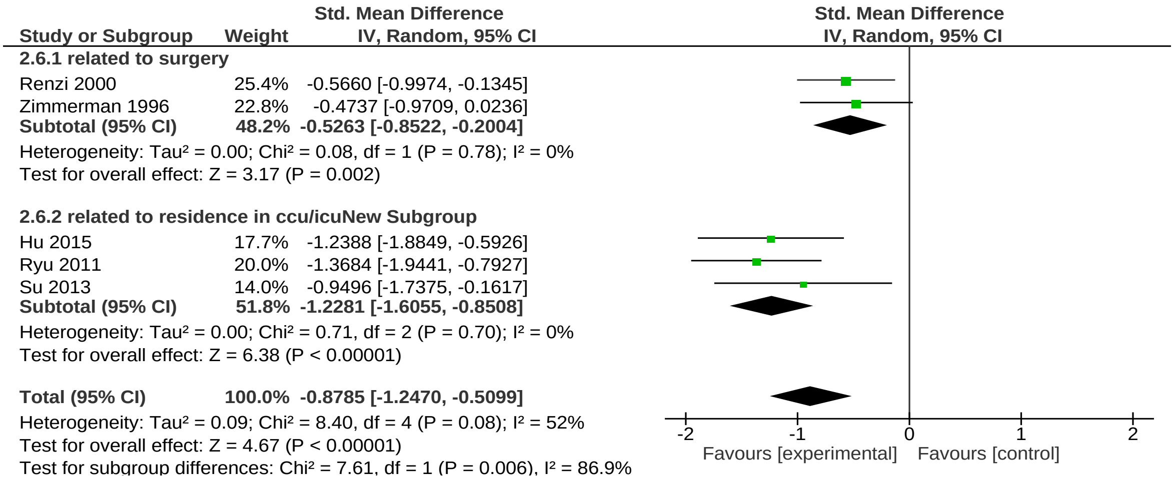
Table 6 Subgroups of sleep disturbances

Sleep disturbances_subgroups (Total sample= 723, N.study= 8)		
	Outcome_type	
Groups	Questionary	PSG
surgery related	2	2
icu/ccu	3	2 (1)
sum	5	4

(1) Outcome data from sleep questionnaires

Using SMD with random-effects model, the overall effect showed the significance (P < 0.00001, SMD = -0.88, CI95%= -1.61, -0.85). However, the moderate heterogeneity (P= 0.08, I² = 52%) caused by clinical conditions was taken into account. The moderator analysis was not conducted, since the number of study was insufficient to ensure the power of examination. Otherwise, the subgroup analysis was carried out. The studies were distributed in two subgroups: ICU/CCU-related condition and surgery-related condition. As a result, the heterogeneity within the subgroups was no significant (P = 0.70, I² = 0% and P= 0.78, I² = 0%). The overall effects were estimated, indicating the effective application of music in the subgroup of CCU/ICU (P < 0.00001, SMD = -1.23, 95%CI = -1.61, -0.85), and of surgery-related condition (P = 0.002, SMD = -0.53, 95%CI = -0.85, -0.20), respectively (Figure 14).

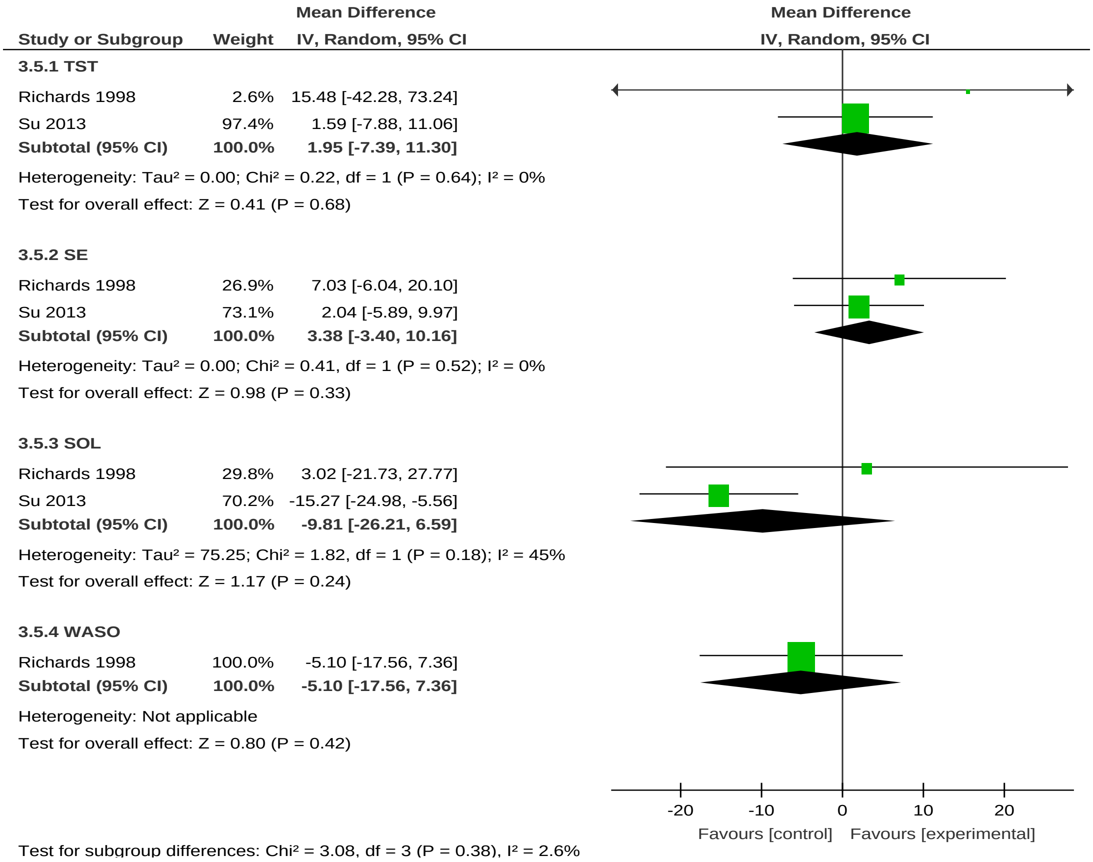
Figure 14 Forest plot of sleep disturbances



(2) Outcome data from PSG

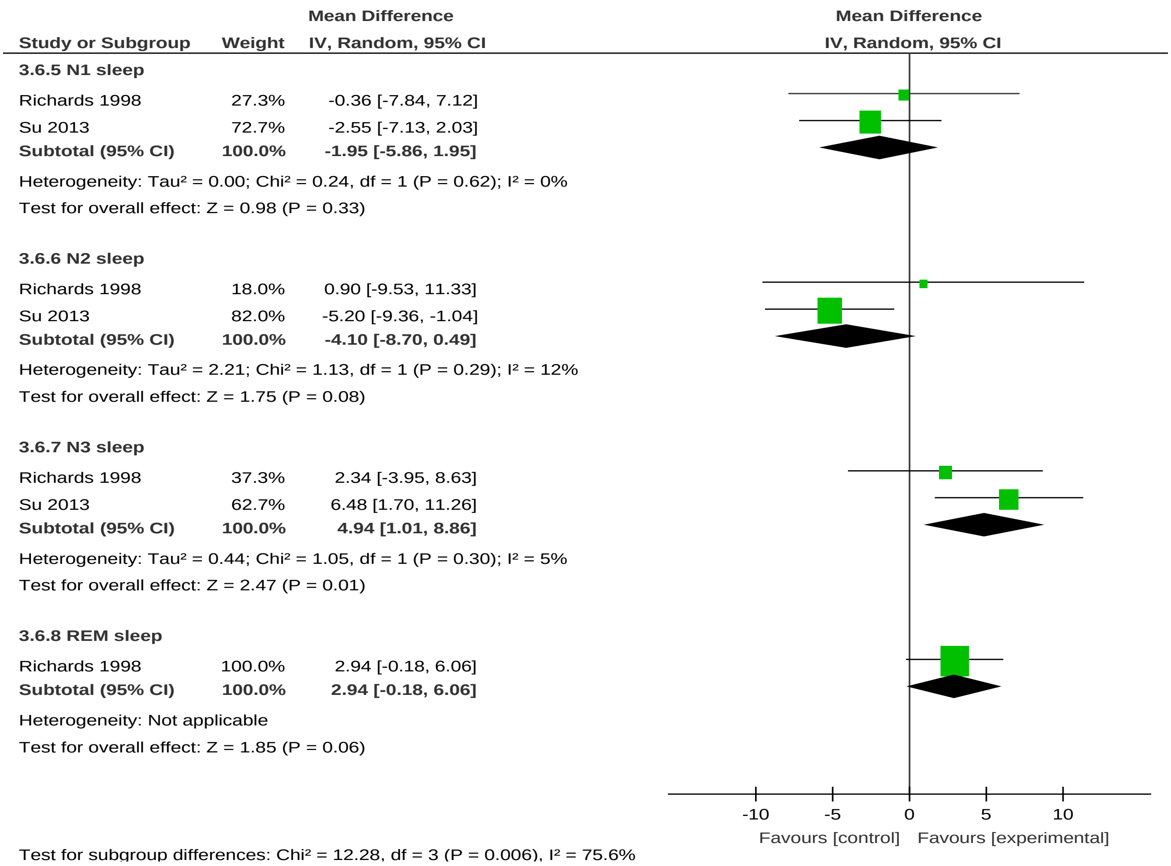
Two studies using PSG measurement focused on patients in ICU/CCU. One study especially included only patients with cardiovascular diseases [73]. The music intervention was conducted only once, so was the sleep quality measured only one night. Because of the same measuring units (minutes), MD was chosen as effect estimator. The other reason was given in advance (Figure 15).

Figure 15 Forest plot of sleep disturbances in ICU/CCU measured by PSG



Generally, the heterogeneity was not important, except that the indicator of SOL appeared a moderate heterogeneity (Chi² = 1.82, P = 0.18, I² = 45%). The overall effect indicated the significance in N3 sleep (deep sleep stage) (P = 0.01, MD = 4.94, 95%CI = 1.01, 8.86). Furthermore, N2 sleep stage (P = 0.08, MD = -4.10, 95%CI = -8.70, 0.49) and REM sleep (P = 0.06, MD = 2.49, 95%CI = -0.18, 6.06) tended to be significant (Figure 15).

Figure 15 (continue)



(3) Studies apart from Meta-analysis

Neander [94] investigated the sleep disturbances in patients (age = 55-81 years) with postoperative nursing, using an ocean-style music improvisation, and estimating the ratio of NREM (N1-N3 sleep stages) to REM sleep in 1-3 days. The result proved that music intervention bettered sleep quality by influencing ratio of sleep stages (the normal ratio of NREM to REM was 70: 30). In addition, listening to a certain music style extended sleep latency ($P \leq 0.01$) and decreased anxiety of patients. The music style mentioned by the author was portrayed as less dramatic in music dynamic and 4/4 beat rather than 4/3 beat. In addition, the music piece was not chosen by patients themselves but by the authors.

The other operation-related study was researched in China by Ma et al. [71]. Totally 200 preoperative patients (age= 16-60 years) were randomly assigned to the intervention group (music with relaxing technique) and the control group (standard care alone). The Self-Rating Anxiety Scale (SAS) contained a sleep-related question responding to four grading answers concerning sleep quality. The music intervention led to more improvement ($u = 5.023$, $P < 0.001$) than the standard care.

4.4.4 Other sleep problems

This category group consisted of three studies of NICU; one study of sleep-related epilepsy; another study of sleep-related breathing disorder. The relevant information was tabled as follows (Table 7):

Table 7 Groups of other sleep problems

Other sleep problems (Total sample= 174, N.study= 5)	
Groups	**Outcomes**
Preterm babys	Infant behav. State
(Sample=113)	Heart rate
(N.study=3)	O2 saturation(%)
	EEG
Apnea	PSQI
(Sample=25)	ESS
(N.study=1)	partner's evaluation
Sleep-related epilepsy	Seizure monitor
(Sample=25)	
(N.study=1)	

Due to important clinical diversities, the meta-analysis was not conducted. More details can be found in the table of study characteristic. Furthermore, their special effects of music on sleep were described as follows.

(1) Sleep-related epilepsy

Bodner et al. [32] focused on the patients with various neurological handicaps, and many with epilepsy. Due to brain seizures presented during nighttime, the individuals suffered commonly from difficulty of sleeping. The particular music piece (Mozart Sonata for two pianos in D major, K. 448) was used for one year (total experiment lasted three years: in the first year, baseline seizure of all participants was measured; in the second year, music treatment was conducted; the third year was to follow-up without music intervention). As a result, the authors found a significant effect (P = 0.024) in the second year and pointed out the persistent effectiveness in the third year (P = 0.0002). Additionally, the study even showed that 24% of patients exposed to music displayed a complete absence of seizures during the year of treatment.

(2) Sleep-related breathing problem

Puhan et al. [95] implemented a randomized controlled trial to assess the effect of didgeridoo playing on the patients with moderate obstructive sleep apnea and snoring. The patients had to learn how to play the didgeridoo and to practice it daily at home for four months. The intervention group showed the less daytime sleepiness than control group (difference -3.0, 95%CI =-5.7, -0.3, P = 0.03). Moreover, the score of apnea index was reduced (difference -6.2, 95%CI =-12.3, -0.1, P = 0.05), so was the partner rating of sleep disturbance (difference -2.8, 95%CI =-4.7, -0.9, P < 0.01). Though the sleep quality estimated by PSQI did not show the differences between groups, regular didgeridoo playing was suggested to be an effective treatment for sleep apnea and it was well accepted by patients.

(3) Sleep development in preterm-infants

Neal's study [96] aimed to observe preterm-infants responding to music intervention compared with ambient noise. The oxygen saturation, heart rate, and behavioral states of totally 41 preterm-infants (32 to 35 weeks' gestation age) were estimated every 30 minutes before, during, and after sound conditions (Brahms' Lullaby). There was no significance between groups over three time points. The effect size showed small either in oxygen saturation (SMD = -0.18, 95%CI = -0.80, 0.43) or in heart rate (SMD = -0.12, 95%CI = -0.50, 0.27). However, the results compared to pretest indicated the significant changes in oxygen saturation ($P < 0.004$, 10 minutes after listening to music), so did the change in heart rate ($P = 0.07$, 10 minutes after listening to music) occurred in individual infants. The Infant's behavioral states showed the significance after listening to music ($P = 0.05$), meanwhile, the infants were aroused slightly and went from quiet sleep stage to active sleep stage.

Olischar et al. [49] observed 20 preterm-infants (≥ 32 weeks' gestation age) responding to the 30-minute music intervention (Brahms' Lullaby). The background pattern and sleep-wake cycle were examined using aEEG (Amplitude-integrated EEG). The results showed no significance between groups. However, the progressive background pattern underlying the developing sleep-wake cycle was found in infants after being exposed to music. In addition, the length of quiet sleep and interval between epochs of quiet sleep became much longer in some preterm-infants in the intervention group.

Schlez et al. [72] administered a within-subject, crossover design using harp music intervention with kangaroo care compared kangaroo care alone. In this study, totally 52 mother-baby dyads (32 to 37 weeks' gestation age) were randomly distributed into one of the groups for 30 minutes. The results indicated no significance in testing infants' heart rate, oxygen saturation, respiratory rate, and behavioral state between groups. Otherwise, music intervention was much beneficial to maternal anxiety state ($P < 0.01$).

4.5 Publication bias

To evaluate reporting bias, the studies with sleep questioners (12 from the group insomnia, five from sleep disturbances, total number of studies = 17) were analyzed through Begg and Egger's tests for detecting plot asymmetry. These two types of test involve rank correlation model and regression model by setting SMD against standard error as parameters. They were conducted in RStudio with a particular meta-analysis' package "metafor". Due to the considerable heterogeneity among studies ($I^2 = 91.75\%$, $P < 0.0001$), Egger's test pointed out the present asymmetry of funnel plot ($p < 0.0001$), so did Begg's test ($P = 0.0018$) (Figure 16). In addition to publication bias, asymmetry of funnel plot could also be caused by high heterogeneity among studies. Thus, the influence of moderators investigated in advance was concerned. Three approaches were implemented, so that the modifiers could be better controlled: the first was to put the studies of cancer aside, which caused the substantial heterogeneity among studies, and then examine the funnel plot asymmetry again. In the first approach, Egger's test (P = 0.0253) was showed significance, so was in Begg's test (P = 0.0590) (Figure 17).

The method of trim and fill was contained in this "metafor" package and recommended to predict how many studies should be added in to balance the funnel plot. The result was showed as follows. Four studies were likely missing on the right side (Figure 18).

Figure 16 Funnel plot based on 17 studies

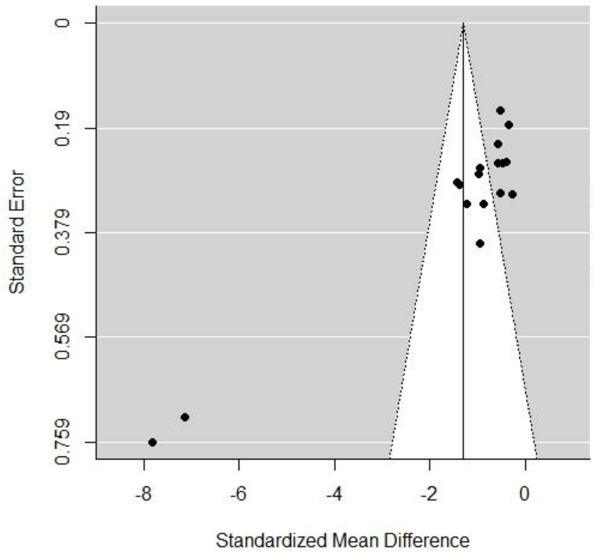


Figure 17 Funnel plot based on 15 studies (without two outliers)

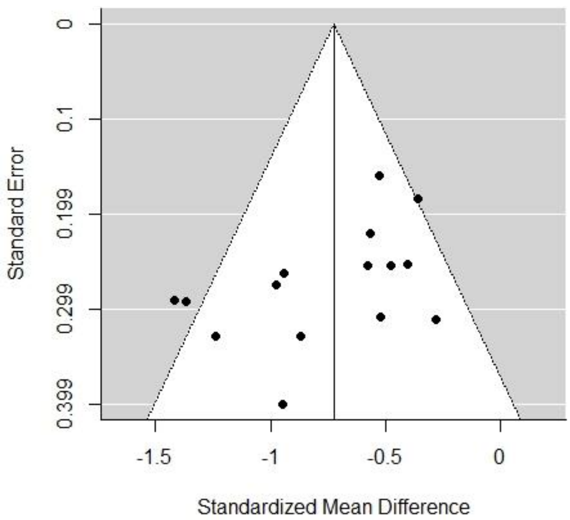


Figure 18 Number of missing studies added into 15 original studies

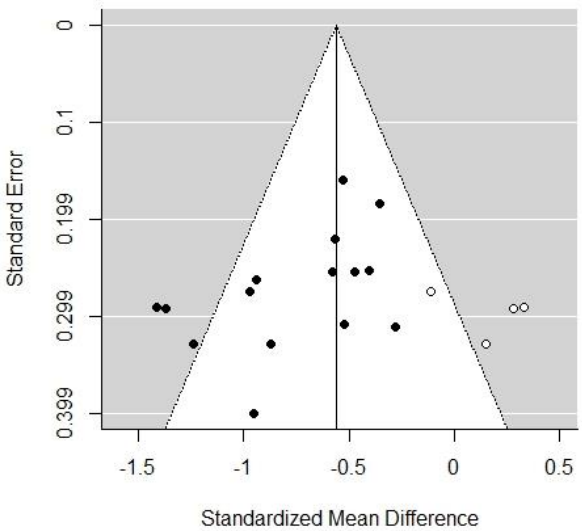
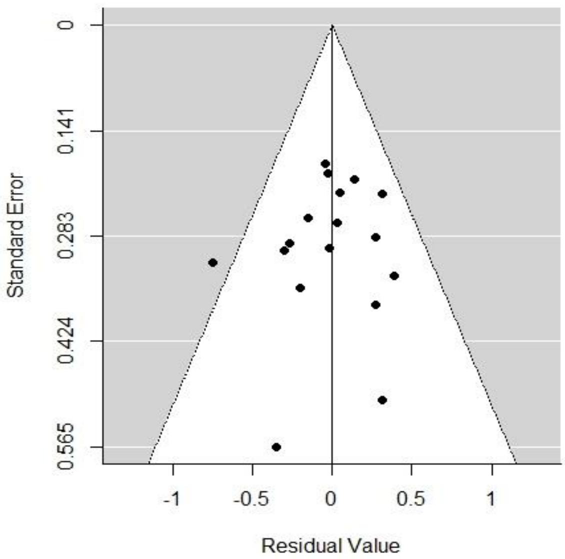


Figure 19 Funnel plot combined with the modifier (clinical conditions)



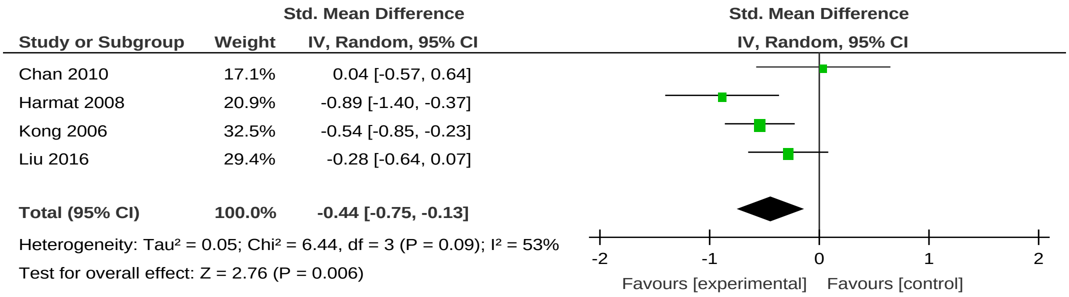
The second approach was to combine the meta-regression model of 17 studies with the potential modifiers. The “Metafor” package provides a particular function for including the impact of modifiers on the original meta-analytic fixed- and random-effects model. In the second approach, the meta-regression model was modulated by mixed-effects model, in which the modifier “clinical conditions” was counted in and the residuals were used to predict SE. The distribution of funnel plots showed no significance in examining asymmetry through Egger’s test (P = 0.2194) (Figure 19).

The third is to observe the study groups: insomnia (unspecified) and sleep disturbances, respectively. Total eight studies assessed sleep quality with questionnaires in the group of insomnia (unspecified). The distribution of funnel plots was likely symmetrical through observation. Owing to the small number of study (N=5) in the group of sleep disturbance (ICU/CCU/surgery), the Egger’s test may be not powerful for estimation of asymmetry. Hence, the asymmetry of funnel plot was difficult to estimate.

4.6 Secondary outcomes

There were eight studies providing mood-related outcomes, including SCL 90, STAI, BDI, SDS, and MADRS (Refer to LIST OF ABBREVIATIONS). According to the sections of grouping in advance, four studies categorized by insomnia (unspecified) were examined as significant in the overall effect (P = 0.006), but moderate heterogeneity (I^2 = 53%, P = 0.09) (Figure 20). Due to the substantial heterogeneity among the remaining studies (N=4), they were merely distributed in the appropriate groups, including insomnia (due to chronic disease) [38, 90], sleep disturbances after surgery [41], and sleep-related breathing problem [95]; but their effect sizes were not merged.

Figure 20 Emotion-related outcomes in patients with unspecified insomnia



There were six studies reporting pain-related outcomes using VAS and VRS. Likewise, the grouping of studies was firstly conducted. In the group of insomnia (due to pain disorder) (N=2), the overall effect showed P-value of 0.07 with moderate heterogeneity (I^2 = 51%, P = 0.15) (Figure 21). The remaining studies (N=4) were not combined, because of the substantial heterogeneity (Figure 22).

Figure 21 Pain-related outcomes in insomniacs (due to chronic diseases)

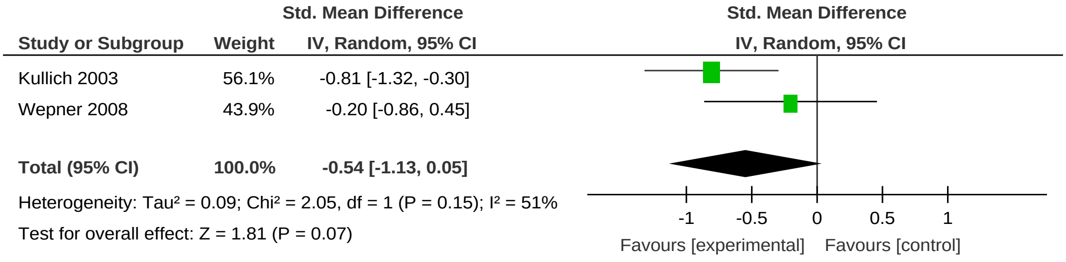
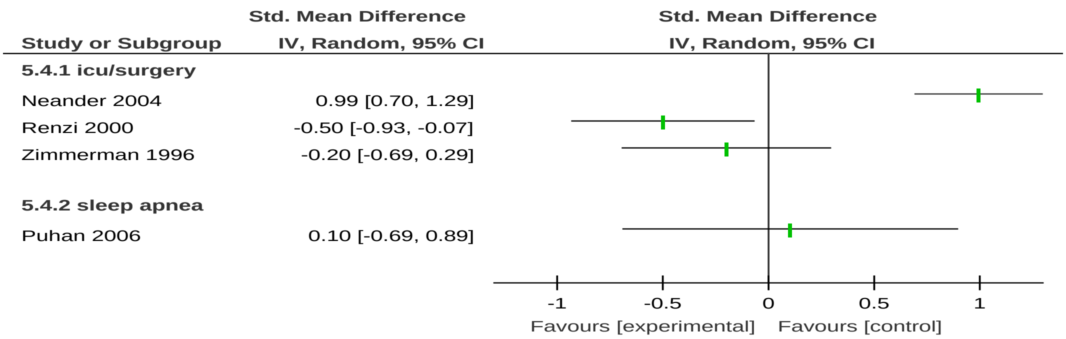


Figure 22 The remaining studies with pain-related outcomes



4.7 Investigation of music characteristics

In a view of clinical perspective, it should be important to know what kind of music has function. This kind of questions could be defined by various music characteristics. However, the included studies provided more outward manipulations of music intervention, e.g. length, surrounding conditions than inward elements of music, e.g. Tempo, key, scale, music form. Hence, this current review could only exhibit a qualitative description of music characteristics, according to the previous study-grouping (Table 8). The music genres of included studies were categorized into traditional style (Indian model, Thailand traditional music etc.), western classic music (Mozart, Beethoven etc.), popular music (Jazz, blue, new-age music etc.), and compound music pieces (mixed styles). Due to the shortage of music-related information, more music items (parameters), e.g. music form, performance, were not available for further analyses.

4.8 Summary of finding table

Furthermore, all of the finding evidence was evaluated by GRADE approach. In addition to the estimate of risk of bias and publication bias [97–99], the GRADE handbook introduces the other three items for criticizing the providing results, including inconsistency, indirectness, and imprecision.

Inconsistency refers to how wide the point estimates look like and whether they have overlap between each other, and whether the statistical tests of heterogeneity, I^2 und Chi^2 (< 0.05), indicate the important variation among the point estimates. The indirectness of evidence refers to how the providing results are applicable to the certain clinical question [100, 101]. The more clearly the question was expressed, the simpler the author's judgment could be made. In the current review, for instance, a special music approach "signing bowl" was used in a study. Though this special approach was counted in the perceived music intervention, it was unlike the other music approaches (e.g. listening to music CD, live music). Therefore, it led to the strong variation responding to the point estimate and might reduce the directness of overall evidence as well. Once the judgment was made, the evidence was downgraded by one or two levels with serious or very serious interpretation.

The imprecision of evidence is relatively complex. It requires some particular criterion. According to the suggestion of GRADE guideline and Cochrane handbook [55, 89], the upper and lower limit of 95% confidence interval was initially examined, whether the 95%CI crossed the threshold of null effect. Otherwise, this current review followed the explanation of effect sizes based on Cohen's definition [102], where 0.2 was interpreted as small effect, 0.5 as medium, and 0.8 as large. Additionally, an effect size of 1.30 supplied by Rosenthal was defined as very large [103]. For instance, a pooled 95% confidence interval was located between 0.3 and 0.98. This range containing the medium and large effect size could elucidate the imprecision of evidence. Thus, downgrading for imprecision was made. Subsequently, the Optimal Information Size (OIS) was calculated as the second indicator [104]. Therefore, two steps were followed: 1) did the 95%CI cross null effect or different levels of effect size? 2) When the 95%CI was not crossed, was an optimal information size met?

To obtain the optimal information size (OIS) for continuous data requests a calculation of sample size. The basic rule was stated in GRADE Handbook 2013:

> *The total number of patients included in a systematic review is less than the number of patients generated by a conventional sample size calculation for a single adequately powered trial, consider rating down for imprecision.*

Moreover, the on-line sample size calculator (http://www.sample-size.net/means-effect-size/) was employed. The property of $\alpha = 0.05$ and $\beta = 0.2$ thresholds were appointed. The sample size was computed through keying in the mean difference suggested by other relative studies and the appreciate standard deviation. The mean difference could also be the difference (Δ), which researchers wish to detect. Once the real sample size was larger than the sample size calculated, the effectiveness could be ensured. The OIS was met consequently. Nevertheless, the handbook reminds of downgrading the evidence, whenever the number of event is less than 400. The summary of finding table was exhibited in Appendix F, so were the relevant explanations.

Table 8 Musical characteristics

Patient groups	Study ID	Duration	Length of music	Music intervention	Genre of music
insomnia	Chan 2010	3 weeks	30-45 min.	slow and flowing meditative, Chinese classical, western classical and western modern-Jazz.	mixed style
	Chang 2012	4 days	45 min.	slow, minor tonalities, smooth melodies, no dramatic change	mixed style
	Deshmukh 2009	4 weeks	45 min.	flute-based compositions were based on the Indian classical music: raags Bahar, Bihag, Mishra Pilu and Malay Martutam	traditional
	Harmat 2008	3 weeks	45 min.	relaxing classical music including some popular pieces from Baroque to Romantic	western classic
	Kong 2005	2 weeks	40 min.	Vibroacustic therapy with "Gong" tonality	traditional
	Kullich 2003	3 weeks	25 min.	,,Entspannung bei Schmerzen", Mentalis Verlag, ISBN: 3-932239-95-4).	popular
	Lafci 2015	7 days	21:00-01:00	The music intervention consisted of Turkish soft Music (Hicaz and Zirefkend music)	traditional
	Lai 2006	3 weeks	45 min.	sedative music contained west synthesizer, harp, piano, orchestra, Jazz music, and Chinese Orchestra.	mixed style
	Lee 2015	2 weeks	30 min.	NA	mixed style
	Liu 2016	2 weeks	30 min.	Symphonic music (from Taiwan songs), wesrern classical music(Bethoven: Für Elise; Debussy: Preludes), nature sounds, lullabies(Brahmus, little star)...	mixed style
	Mottaghi 2015	4 weeks	45 min.	A CD containing a sedative music for nights is used before going to sleep, an energetic music for mornings to be alive and vital	mixed style
	Reinhardt 1999	13 days	30 min.	Music was perfomed by a chamber orchestra included synthesizer and Messo-sopran. A lullaby-like music style.	popular
	Shum 2014	6 weeks	40 min.	Soft, instrumental slow sedative music without lyrics,	mixed style
	Suwansathit 2015	1 night	30 min.	Style of thai light music	traditional
	Wang 2016	3 months	30-45 min.	169 pieces of music were recorded in the MP3 player.60-80 beats per min. Music styles included Chinese instrumental classic, Western classic, nature sounds, classical songs without lyric.	mixed style
	Wepner 2008	4 weeks	30 min.	Crystal Singing Bowls with sound a, f' or g'	NA
ICU/CCU/ surgery	Hu 2015	2 days	30 min.	relaxing music during the postoperative nights	mixed style
	Ma 2004	1 day	NA	quiet music style for relaxation assisting sleep hygiene information	mixed style
	Neander 2004	7 days	19:00-6:30	"Low Swin", a quiet music style of improvisation. "Paul Winter Consort", an orchestra music with wind instruments, guitar and percussion.	popular
	Renzi 2000	1 day	30 min.	The use of relaxation techniques "guided imaging" (GI) consisted of a soft, "new-age-lke" musical background and a relaxing text	popular
	Richards 1998	1 night	7.5 min.	Music relaxation program consists of progressive muscle relaxation, mental imagery and background music. The music was Water Spirit from the album Water Spirit by Kim Robertson	popular
	Ryu 2011	1 night	52 min.	Delta-wave & Alpha-waves. Nature Sounds, Delta Wave Control Music, Goldberg variations, Nature Sounds	mixed style
	Su 2013	1 night	45 min.	4 musical pieces were composed of sedating piano music with a smooth rhythm to achieve a relaxing effect.	popular
	Zimmerman 1996	3 days	30 min.	Country Western Instrumental, Fresh Aire; Winter into Spring, Prelude and Comfort Zone. All of them had the soothing style of music.	popular
preterm baby	Schlez 2011	1 day	30 min.	Live harp music comprised simple improvised melodies in the style of lullabies with soothing and repetitive wordless melodic lines, using major and harmonic minor modes with Jewish and Arab music	traditional
	Neal 2008	NA	10 min.	Brahms' Lullaby	western classic
	Olischar 2011	1 day	20 min.	Brahms' Lullaby.	western classic
sleep related epilepsy	Bodner 2012	1 year	8.5 min	Mozart Sonata for 2 pianos K.448	western classic
sleep-related breathing	Puhan 2006	4 months	20 min.	Didgeridoo playing	traditional

N/A: not available

5 Discussion

5.1 The effectiveness of music on insomnia

According to the finding in this current research, listening to music for two to four weeks has a positive impact on patients with insomnia (PSQI > 5). Elderly people (> 60 years) can especially benefit by listening to music for three to four weeks. As the included studies suggested, listening to soft and slow music for about 30-40 minutes regularly before bed-time could be a supporting treatment for insomniacs. Concerning the dosage of music, the frequency of weekly use was testified in this research as non-significance; even so, it should be still advised, that listening to music over twice a week may strengthen the adaptation of human brain quicker than listening to music only once a week. In a few studies, in which insomnious patients have suffered from long-term diseases, such as depression, chronic pain disorders, music intervention should be used better more often, at least for one month. Furthermore, music can certainly work on sleep quality in insomniac cancer patients by listening to music continuously for one to two weeks. This finding was based on two studies. Lafci and colleagues [78] reported a randomized control design, using instrumental music with Indian classical music style for seven days consecutively, listening once a day before bed time. Lee and colleagues [90] provided music pieces chosen by participants twice a week for 14 days. Both of the two studies were examined as not significant in the test of heterogeneity ($P = 0.54$, $I^2 = 0\%$), showing the almost similar magnitude by standardizing their mean differences.

In this research, the studies using PSQI as outcome assessment were estimated with SMD and then with MD. Because the MD provided the absolute reduction reflecting on PSQI. Concerning this, a few studies have been reported about the minimal clinically important difference (MCID) of PSQI [105]. The minimal change of three was defined in Hughes' study [106]. However, Lu's study [107] indicated the minimal change of 1.54 based on a randomized control study of Chinese medicine [108]. Compared to this current research, patients with insomnia (unspecified) obtained a reduction of two points, which was beyond the MCID in Lu's finding. Likewise, the elderly people listening to music after three to four weeks achieved 1.92 points fewer than control. It also exceeded the MCID.

As mentioned in some previous studies, listening to music for three weeks was suggested [109]. Based on the finding of this research, the effect of music became already significant in 14 days. Though there was a study showing a tardy effect [110], the other studies indicated consistently the significant effect ($P = 0.69$, $I^2 = 0\%$). Thus, this finding implies that music treatment at least two weeks should be beneficial to patients with insomnia. The frequency may be suggested five to seven times a week. Moreover, the treatment of 21 to 30 days could obtain the steadier effectiveness of music. Toward the outcomes in two and three months, it could be deduced that the quality of sleep must be improved due to the cumulative effect of music. Yet, in this current research, music treatment in two months presented high heterogeneity. It could be explained by the different manipulations of music intervention; for example, in Wang's study, participants chose their preferable music every night from a database with total 169 music pieces [51]. Suppose some people changed the music piece every day, it might not be suitable for the adaptation of brain. As a result, this study displayed a tardy change compared to other similar study designs. In order to detect diversity of clinical music application in a time period of one month or longer, more relevant studies need to be done henceforth.

Regarding the results of PSG, no significance showed among different sleeping parameters of PSG. Some parameters indicated a slight positive tendency; for instance, N1 sleep of insomnic patients was shortened (P= 0.08, MD= -1.49, CI 95%= -3.41, 0.16), N3 sleep in ICU/CCU became longer (P= 0.01, MD= 4.94, CI95%= 1.01, 8.86). However, the heterogeneity and imprecision according to GRADE were evaluated as low. More insomniac studies measured by PSG should consider the longer treatment duration, such as 14 days.

5.2 The effectiveness of music on sleep disturbances

This finding positively supports the efficiency of music in improving patients' sleep during staying in ICU/CCU and surgery-related conditions. The quality of sleep can be restored after listening to music 1-3 days. Due to the small sample size, more potential variables could not be concerned (e.g. type of surgery, phase of surgery: pre-, intra-, postoperative). Therefore, this result could not be generalized to all patients in ICU/CCU/surgery-related conditions yet. However, side-effects were not found and all included studies had a consistent conclusion that music can be a supportive treatment for patients' sleep in ICU/CCU/surgery-related conditions.

Regarding the finding of PSG, although one may criticize its validity due to the small sample size, it may be still meaningful to have a proof about the potential benefit of music for more clinical consideration. In light of a research report [22] about sleep in intensive care published in the American journal of respiratory and critical care medicine, abnormal sleep in ICU characterized by using PSG was demonstrated with prolonged sleep latency, increased arousals, N1 and N2 sleep stage, decreased sleep efficiency, N3 sleep stage (deep sleep) and REM sleep. In this current research, listening to music for one to three days indicated a positive change on PSG indicators, especially in shortening N2 sleep stage, increasing N3 sleep stage, as well as prolonging REM sleep. However, the given evidences were interpreted as the imprecision owing to the broad confidence intervals. In order to upgrade the quality of evidence, more relevant studies will be needed. The researcher should add the duration days of using music to one or two weeks, testing more differential music styles, and focusing more on music function in changing N2, N3, and REM sleep.

5.3 The effectiveness of music on other sleep problems

According to some individual studies, the positive effectiveness of music appeared furthermore in the sleep-related breathing problems, sleep-related epilepsy as well as the sleep of preterm-babies. For the patients with sleep-related breathing problems, playing didgeridoo (a wind instrument developed by Indigenous Australians [111]) regularly for four weeks definitely improved the sleep-related breathing disorders. For the patients with sleep-related epilepsy, listening to some particular music, e.g. Mozart's Sonata for two pianos, in D major, K448, was examined as helpful in reducing the seizure occurrences. Concerning these two kinds of sleep disorders, the clinician should consider listening to music as an assistant therapy, in order to increase the number of relevant studies. Moreover, listening to music might promote the development of sleep in preterm-babies, although the results showed inconsistent among the collected studies. Further, the researcher should think more about the amplitude-integrated electroencephalography (aEEG) as the measuring method in preterm-babies, in order to obtain a more precise and detailed report.

5.4 Analysis of music parameters on clinical perspective

According to previous studies, the selection of music and the therapeutic implementation were reported as critical issues. The selected music was almost described as slow, relaxing, seductive style with smooth melodies, without dramatic change, and without lyric. A tempo of 60-80 bpm with 30-40 dB was suggested. Listening to music on the bed time for at least 30-45 minutes was mostly conducted in the included studies. It was also mentioned in previous research that the individual's preference of music could lead to more positive influence [112]. However, the subject's musical preference might not always enhance the effect on sleep quality [113]. Music selection usually corresponds to cultural background of the individual. For instance, Lafci et al. [78] used traditional Indian music with special scale mode, which was familiar to all recruited Indian people. They felt more comfortable and secure in spite of individual music preference. However, it is definitely complex to identify what kind of music piece has universal effectiveness for what kind of patients. In the other aspect, a music piece is composed of different music factors (called also: parameters); through these music factors, the music piece is characterized and then works on people. Concerning musical characteristics, it has been discussed that more percussive elements and chord changes may bring about muscular tension as well as energize mentality. In contrast, the sustained melody with identical scale pattern could produce such kind of contemplative emotion. Furthermore, the vocal music might be less simulative than instrumental music [114]. Yet, most of the studies included in this current research used instrumental music. In the past decade, music effect was constantly proved by neurological imaging technique, which showed that music listening and playing could activate the different brain areas for getting somehow dynamic impact on psychic and physical mechanisms. Besides, the relaxing effect lies in increasing alpha waves, which could be induced by music. Listening to smooth music passage repeatedly could intensify sensory adaption. On the base of those evidences, to know more about the function of music underlying differential musical factors as a description of musical nature could offer a more specific guideline for clinical utilization.

Due to the limited information about music parameters, only the music genre and style were investigated through a moderator analysis. In the future, more details of music factor should be considered before using music as a healing medium.

5.5 The whole quality of evidence

In this current review, the whole quality of evidence was not strong enough, especially in selection bias and performance bias. A lack of random sequence generation and allocation concealment weakened the quality of evidence. Most of the researchers could not accomplish double-blind design, because of the nature of music intervention. Therefore, it is important to note that some studies showed somewhat large difference especially between the experimental group and the comparison with non-treatment. This a bit large difference could cause the substantial heterogeneity among studies. Thus, it is assumed that the large difference happened in the trials, where participants and care provider were not masked. In this regard, it is suggested for the prospective studies that the control group may use a placebo setting, such as listening to an audio book with earphones or an audio tape of relaxing instructions with earphones. It can minimize the performance bias. On the other hand, this performance bias may be only avoided in comparison with different types of music. For example, in a trial evaluating music therapy, participants were informed that the study intended to test two types of music intervention, whereas the true hypothesis was that music with certain musical portraits was considered effective and the other music type from random chosen was considered placebo. Moreover, in order to enhance the reliability of music effect on sleep research, blinding of outcome assessor should be better implemented, so does random sequence generation as well as allocation concealment. Those experimental operations mentioned need to be achieved and recorded exactly.

According to GRACE handbook, the imprecision of whole evidence needs to be improved. It could be associated with the insufficient sample sizes, which were minimized due to subgroup-analysis.

5.6 Supplement of other relevant reviews with meta-analysis

Three review articles [50, 52, 53] related to music effect on sleep were retrieved and explored. (Table 9). De Niet’s study was published in Journal of Advanced Nursing; Wang’s study in International Journal of Nursing Studies, and Jespersen’s study in the Cochrane Library. The processes of study selection in these review-articles were conducted carefully by two independent reviewers. The important inclusion criteria among these three articles were firstly outlined below, and then compared to this current study.

Table 9 Four relevant reviews with meta-analysis

Studies	Search update (until)	Populations	Interventions	Comparators	Sleep outcomes	Number of studies (sample)*
De Niet et al. [50]	July, 2008	Adults with sleep complaints	Receptive music method	Control (Non-music / standard care)	Only sleep questionnaire included	5 studies (n = 308)
Wang et al. [53]	2012	Adults with acute and chronic sleep disorders	Receptive music method	Control (Non-music /standard care)	sleep questionnaire & Polysomnography (only "sleep efficacy" included)	10 studies (n = 557)
Jespersen et al. [52]	May, 2015	Adults with Insomnia	Receptive music method	Control (Non-music /standard care)	sleep questionnaire & Polysomnography	5 studies (n = 264)
Huang 2017 (current)	April, 2017	People with sleep disorders (no age limit)	Receptive & active music method	Control (Non-music / placebo /standard care)	sleep questionnaire & Polysomnography	20 studies (n = 1304)

* Number of studies showed the number included in the meta-analysis

Since the in- and exclusion criterion differed from each other, the judgments of qualified studies varied among the review authors. De Niet [50] included finally five studies [74, 76, 115–117] for a meta-analysis. These studies were also included in Wang's et al [53]. Besides, Wang et al. added the other five studies [1, 62, 92, 109, 118] into a meta-analysis. A few of them were published after 2009. Jespersen [52] reduced the numbers of eligible studies to five; of which three studies [74, 76, 115] were found in the forehanded reviews, and the other two studies [77, 119] were newly added to the meta-analysis. Compared to other three review-articles above, this current study was involved in 21 relevant studies and synthesized them in the meta-analysis. In addition to 21 studies, there were still eight randomized controlled studies identified as eligible and described in details. However, Hernandez-Ruiz's [117] and Jespersen's [119] studies qualified in other reviews were excluded from this current study, because they were both clinical control trials without randomized distribution. These trials, so called quasi-randomized, did not match the current inclusion criteria.

Except this current study, the other review-articles concentrated the populations on adults aged 20-80 years with difficulty in falling asleep; especially in Wang et al. [53] and Jespersen et al. [52], where Insomnia diagnosed through Pittsburgh Sleep Quality Index (score >5) was a necessary inclusion criteria. Three review-articles rejected the intervention with active music techniques. Yet, this kind of intervention was included in this present study. Besides, Wang et al. and Jespersen et al. contained both subjective and objective assessments of sleep quality, so did this current study. Nevertheless, the number of study with objective assessments was not many. Therefore, Wang et al. in 2014 merged the two relevant studies assessed by PSG in the analysis, where the other studies were assessed by sleep questionnaires. As a sequence, merely the "sleep efficacy” (one of PSG indicators) was chosen and combined with the outcome of sleep questionnaires. It could be a real loss in obtaining more clinical knowledge about the physical change responding to music intervention. In contrast to Wang’ study, Jespersen et al. in 2015 separated the types of outcome assessment and then displayed the one study with PSG outcome individually. Furthermore, this current research added more relevant studies, categorizing their possible contributing factors, and splitting them into the appropriate subgroups according to different types of outcome.

5.7 Limitations and suggestions for the future research

This current research explored abundant databases without the limit of language. Consequently, it was found that many qualified studies (at least 40 studies) retrieved from Chinese databases were not indexed in any other international databases (e.g. PubMed). As well, most of them were written only in Chinese. It caused the difficulty in the process of pair-review. There was only one Chinese-speaker among the co-workers. Considering the transparency in the research, only the Chinese study indexed in the international database was included. With regard to the further research, people may think about searching in databases of different languages and simultaneously setting the stricter criterion of ex- and inclusion.

In general, the quality of included studies was not perfect enough, since the nature of music intervention could not satisfy the requirement of double blinding design. As to this shortage, single blinding and randomized executions should be better done strictly in the future research in order to enhance the total quality of study.

Furthermore, the current research included a broad patient population with various kinds of sleep problems. Henceforth, the primary problem before the combination of effect sizes was to deal with the considerable heterogeneity. It was much reduced by conducting some pertinent analyses (e.g. meta-regression, subgroup-analysis). However, as a consequence of subgroup-analysis, the number of people in each subgroup became small (< 400 suggested by GRADE guideline). It could increase the probability of spurious effect (type I error), meanwhile, the insufficient sample size could decrease the power of test (type II error). Therefore, the significant result reported in subgroups of this current research must be seriously considered. Despite those possible problems, the subgroup-analysis did minimize the present heterogeneity, so that the evaluation of effect could be ensured; more clinical hints as well as music applications could be provided.

In most of the studies, insomnia was not defined carefully, so was the possible trigger of insomnia not indicated, either. It might bring about the unclarity in categorizing studies into suitable groups. This issue is a general problem presenting in sleep research. To identify a diagnosis of insomnia is quite complex, because the pathological mechanisms of insomnia may require a serial clinical documentation, such as medical history of the patients, sleep log. The other difficulty is to match the subjective complaint of the patients with their physical signs, which might give more perspectives in the understanding of the music effect on sleep disorders. Seeing this, a multi-method assessment approach to sleep quality and quantity should be concerned in the future research.

In spite of this shortage of diagnosis, this current research only used a common standard for categorizing the studies. On the basis of the subjective complaint, the score of PSQI higher than five and the possible cause of insomnia were both taken into account.

More limitations might be given in the inference of effectiveness. Some studies indicated the cumulative effect of music showing in 14 days and in 21-30 days. This cumulative effect might attribute to the repeated measure; it could not be eliminated in the subgroup-analysis. Besides, the result of PSG showed the slight change responding to sleep time. As mentioned beforehand, it could be due to the short duration of treatment. In order to prolong the duration of treatment, more convenient and comfortable sleep measuring tool rather than PSG should be applied to the physical documentation of sleep, such as Cardiopulmonary Coupling (CPC) [120].

In addition, the publication bias was examined based on a part of studies due to the consistent measuring unit. Nevertheless, the considerable heterogeneity and somewhat extreme studies had a strong impact on the asymmetry of funnel plot. Therefore, this current research applied the trim and fill method suggested by Duval [88] to predicting the missing number of studies. This approach could be only regarded as a simulation of the expected result responding to publication bias. It could not increase the validity of real effectiveness.

The included studies illustrated mostly the “external” manipulation of music intervention, lacking in “internal” description of music used (the content of music). Therefore, more music-related factors for dosage of music medicine could not be explored.

6 Conclusions

Music, as known, is a kindly, convenient and cost-effective healing medicine. Beyond those properties, this current study illustrates an up-to-date utilization of music in different characteristics of patients underlying sleep disorders. It lends evidences to support that music intervention can improve the sleep quality of insomniac and enhance the health of patients in ICU/CCU or in surgery-related condition. The following practices are deserving of being recommended:

(1) The practicing physician can definitely use the advantage of music for facilitating the sleep quality of insomniac, regardless of different clinical conditions or pathological factors. (Nevertheless, thinking of the different clinical conditions and pathological factors might point toward a more specific treatment and strengthen clinical application of music in further details.)

(2) Two to three weeks should be suggested as the standard treatment duration for adults with insomnia (PSQI >5).

(3) Concerning the sleep quality in ICU/CCU or surgery-related condition, patients could benefit from listening to music for one to three days.

(4) The listening time-point should be generally arranged for 30-40 min. before night sleep. According to some special programs, listening to music once in the morning and once in the evening could help people obtain a relaxing and regular lifestyle.

(5) Although the correlation between treatment frequency and effectiveness was not found in this research (due to shortage of study number), the common advice, based on the literature retrospection, should be better more than once a week.

(6) Although the contents of music, such as tonality, melody, form, timbre of music could not be verified in this research as much (due to the insufficient information of music intervention), the musical characteristics should be related to the quiet, sedative, slow, relaxing, and repeatedly style. Furthermore, the melody could be better without lyric and could have less change in dramatic expression. A more expectation is to have the tempo of music synchronized with the heart rate (about 60-80 bpm).

(7) The individual preference of music should be less concerned. Instead of this, the researcher or physician should prepare the music selection with suitable properties beforehand and should be aware that the certain music piece (or a CD with collected music repertoire) has to be listened regularly on the appointed time. It must be avoided providing the participant a mp3-player included too many music pieces (e.g. over 100 pieces). Thus, it could prolong the adaptation of brain and might minimize the efficacy of treatment.

Furthermore, a general consideration should be given to the clinicians that the effectiveness of music could vary among studies due to the diversities of clinical condition. For example, the patient with depressive diagnosis might need longer treatment duration. For such kind of patients, listening to music is suggested for at least one month, so is for the patients with pain disorders. Furthermore, the cancer patients can obtain more significant change than others with chronic or mental disease. However, this finding requires more supporting evidence.

Finally, this research provides a clearer perspective on practical application of music in patients with sleep disorders by means of assessing the objective and subjective sleep measurements and displaying music approach in different sleep-related problems. Although the effect of music on sleep development in preterm-infants was not significantly reflected in using subjective infant-behavior questionnaires, some individual studies (e.g. the study of aEEG) still indicated that music could support preterm-baby in their early development stage.

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Appendix A: Searching technique

Pubmed (69)

#1 sleep OR sleeping OR sleep* OR sleep disorder OR sleeping problem OR insomnia OR hypersomnia OR Nightmares OR sleep-wake OR Sleep terror OR sleep apnea OR restless legs syndrome OR Sleepwalking OR Sleep [MeSH Major Topic]

#2 music OR singing OR improvisation OR music [MeSH Major Topic] OR music therapy OR music intervention OR music medicine

#3 randomized controlled trial [Publication Type] OR random* OR controlled clinical trial [Publication Type]

#4 ((#1) AND #2) AND #3

EMBASE (Ovid) (68)

#1 (sleep or Sleeping or sleep* or sleep disorder or sleeping problem or insomnia or hypersomnia or Nightmares or sleep-wake or Sleep terror or sleep apnea or restless legs syndrome or Sleepwalking).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (mp=Map Term to Subject Heading)

#2 (music or singing or improvisation or music therapy or music intervention or music medicine).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (mp=Map Term to Subject Heading)

#3 (randomized controlled trial or random* or controlled clinical trial).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

#4 #1 and #2 and #3 (90)

#5 #4 and "Journal: Article" [Publication Type] (57) and "Journal: Conference Abstract" [Publication Type] (9) and "Journal: Conference Paper" [Publication Type] (2)

Cochrane-library (48)

#1 sleep or sleeping or sleep* or sleep disorder or sleeping problem or insomnia or hypersomnia or Nightmares or sleep-wake or Sleep terror or sleep apnea or restless legs syndrome or Sleepwalking:ti,ab,kw (Word variations have been searched)

#2 music or singing or improvisation or music therapy or music intervention or music medicine:ti,ab,kw (Word variations have been searched)

#3 #1 and #2

PsyInfo (Ovid) (31)

#1 (sleep or Sleeping or sleep* or sleep disorder or sleeping problem or insomnia or hypersomnia or Nightmares or sleep-wake or Sleep terror or sleep apnea or restless legs syndrome or Sleepwalking).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (mp=Map Term to Subject Heading)

#2 (music or singing or improvisation or music therapy or music intervention or music medicine).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (mp=Map Term to Subject Heading)

#3 (randomized controlled trial or random* or controlled clinical trial).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

#4 #1 and #2 and #3

#5 #4 and "Journal: Article" [Publication Type] and "Dissertation Abstract" [Publication Type]

CINAHL through EBSCOhost (25)

#1 sleep or sleeping or sleep* or sleep disorder or sleeping problem or insomnia or hypersomnia or Nightmares or sleep-wake or Sleep terror or sleep apnea or restless legs syndrome or Sleepwalking

#2 music or singing or improvisation or music therapy or music intervention or music medicine

#3 randomized controlled trial or random* or controlled clinical trial

#4 #1 and #2 and #3

(21= Academic Journal; 3= Dissertation; 1=Conference report)

Web of Science (Web of Knowledge) (30)

#1 Topic=(randomized controlled trial or random* or controlled clinical trial) OR Title=(randomized controlled trial or random* or controlled clinical trial)

#2 Topic=(music or singing or improvisation or music therapy or music intervention or music medicine) OR Title=(music or singing or improvisation or music therapy or music intervention or music medicine)

#3 Topic=(sleep or sleeping or sleep* or sleep disorder or sleeping problem or insomnia or hypersomnia or Nightmares or sleep-wake or Sleep terror or sleep apnea or restless legs syndrome or Sleepwalking) OR Title=(sleep or sleeping or sleep* or sleep disorder or sleeping problem or insomnia or hypersomnia or Nightmares or sleep-wake or Sleep terror or sleep apnea or restless legs syndrome or Sleepwalking)

#4 #3 and #2 and #1

#5 #3 AND #2 AND #1 [Refined by: Document Types=(CLINICAL TRIAL OR ABSTRACT OR MEETING)]

China Academic Journals Full-text Database (108)

#1 (Title/Abstract/subject=music) **AND** (Title/Abstract/subject=sleep ***or*** insomnia ***or*** sleep disorder) **AND** (Abstract=random)

#2 (Title/Abstract/subject=music) AND (Title/Abstract/subject = hypersomnia **OR** Nightmares **OR** sleep-wake **OR** sleep terror **OR** sleep apnea **OR** restless legs syndrome **OR** Sleepwalking)

Journal of Music Therapy:

The typical journals in research field of music therapy, “Journal of Music Therapy” (British Journal of Music Therapy) Nordic Journal of Music Therapy, Australian Journal of Music Therapy, Canadian Journal of Music Therapy, and Music Therapy Perspectives, have been already indexed by MEDLINE.

Appendix B: Kappa statistic for measuring agreement

A simple kappa statistic was calculated. The strength of kappa coefficient between 0.40 and 0.59 shows a fair agreement, between 0.60 and 0.74 points out a good agreement and 0.75 or more reflects an excellent agreement. Kappa coefficient takes the form below:

$$\text{kappa} = P_O - P_e / 1 - P_e$$

(P_o: proportion of observed agreement, P_e: proportion of expected agreement)

As following it shows the record of two reviewers by firstly study selecting.

	Include	exclude	unsure	total
Reviewer 1	43	54	0	97
Reviewer 2	44	53	0	97

Data for calculation of a kappa statistic are inserted into a 2X2 contingency table 1. See below.

		Review author 2					
		Include		Exclude		**Total**	
Review Author 1	Include	41	a.	1	b.	42	g_1
	Exclude	3	c.	52	d.	55	g_2
	Total	44	f_1	53	f_2	97	n.

According the first table, the proportion of observed agreement is:

P_o= (a+d) / n=(41+52) / 97 = 0.9587

Then the proportion of expected agreement was:

P_e= {(f_1 X f_2) /n + (g_1 X g_2) / n} / n = (24.04+23.81) / 97=0.4932

Thus, the kappa was calculated

Kappa=(0.97-0.49) / (1- 0.49)=0.48/0.51 = 0.94117=94%

The result 0.94 reflected an excellent agreement.

Appendix C: Characteristics of included studies

Study	Participants	Interventions	Outcomes	Notes
Bodner et al. [32] Method: RCT	36 participants (IG = 25; CG =11) with heterogeneous neurological impairments, e.g. epilepsy or seizure disorder; stayed in Thad E. Saleeby Center; reported seizure for minimum one year prior to study starting date. Considering a sufficient number of treatment subjects, the allocation was performed according to the 2:1 ratio in the beginning. **Average age** (Mean±SD): 36.11 ± 15.6 years (range: 12-78) **Exclusion criteria:** 1) Participants had no history of seizures, 2) Severe hearing impairment, 3) failure to obtain consent, and 4) subjects exhibited no seizures during any phase of the study.	**Method:** Listening to music **Genre of music:** Mozart Sonata for 2 pianos K.448. It has unique rhythmic structure and long-term coherence, which might be able to stimulate brain's cortex and evoke particular rhythms with anti-epileptiform/anti-seizure properties. **Setting:** Music was presented at periodic intervals with a special sequence: Baseline 9 min.-- Music on 8.5 min.--Wash out 8.5 min.. The protocol was recorded nightly during 9 pm. to 7 am.. A central sound system was used for delivering stimulus to each subject's room and was played with speakers. **Surrounding elements:** Music volum = 60 db **Compared intervention(s):** Control group received standard care, no music exposure.	**Primary:** Seizure frequency were collected hourly. After treatment, seizures were significant reduced.	Sleep-related epilepsy
Chang et al. [118] Method: RCT	50 participants (IG = 25; CG =25) experienced insomnia (PSQI > 5 at screening) for at least one month, and were aged between 20 and 60 years of age **Average age** (Mean±SD): 31.82 ± 11.10 years **Exclusion criteria:** Participants with (1) psychiatric or neurological problems; (2) a history of alcohol/drug abuse; and (3) pregnant or nursing women.	**Method:** Listening to music **Genre of music:** The sedate music was provided. The tempo was ranged from 60 to 85 beats/ min (slow), minor tonalities, smooth melodies, and no dramatic change in volume or rhythm to achieve a relaxing effect. **Setting:** The music was recorded on a CD. The participants were instructed to refrain from consuming alcohol, drugs, and caffeine during the study periods as well as to arrive in the sleep laboratory 1 h before their normal bedtime. (Frequency: 45 min. at nocturnal sleep time for the 4 consecutive days.) **Surrounding elements:** The sleeping room was sound-attenuated, air-conditioned, temperature- and light-controlled single bedrooms. The temperature was ranged from 24° C to 27° C depending on the participants' requests. The background noise levels in the sleep laboratory at approximately 30–35 dB. **Compared intervention:** The control group received standard care.	**Primary:** (a) PSG (b) Self-reported morning questionnaire concerning sleep **Secondary:** (a) Spiel-berger's State-Trait Anxiety Inventory (STAI) (b) Taiwanese Depression Scale (c) VAS for evaluating the enjoyment of music.	Insomnia (unspecified combination with a particular diagnosis or other clinical condition)

Study	Participants	Interventions	Outcomes	Notes
Chan et al. [109] Method: RCT	42 participants (IG = 21; CG =21) at a community services center in Hong Kong were aged 60 or over. Their sleep quality was assessed with PSQI > 5 at baseline. There were 10 subjects (23.8%), who had tried music therapy before. **Exclusion criteria**: Subjects were not eligible if they were deaf; had an altered mental status (e.g., delusions, confusion) or cognitive impairment (inability to understand and follow directions, or inability to read and write); or had a recent death in the family.	**Method**: Listening to music **Genre of music**: Meditative, Chinese classical, western classical and western modern-Jazz. All of them were slow and flowing pieces with 60–80 beats per minute, instrumental, and about 30 min in length. **Setting**: Subjects in the music group were provided an MP3 player with earphones for listening to the music pieces chosen by themselves. The subjects stayed at the most comfortable place. The physiological data and sleep quality were obtained within 5–8 minutes after music listening. (Frequency:30-45 min/ per week for one month) **Surrounding elements:** Some standardized instructions were given to the subjects by the researchers, e.g. listening to music at room temperature; wearing comfortable clothes, turning out the lights and closing their eyes; laying the MP3 at a comfortable volume; not talking, remaining silent… **Compared intervention**: control group was given an uninterrupted rest period with the same relaxing instructions.	**Primary**: Pittsburgh Sleep Quality Index (PSQI) **Secondary**: (a) Geriatric Depression Score (GDS-15) in Chinese short version (b) Systolic blood pressure (SBP) (c) Diastolic blood pressure (DBP) (d) Heart rate (HR)	Insomnia (unspecified combination with a particular diagnosis or other clinical condition)
Deshmukh et al. [38] Method: RCT	50 participants (IG = 25; CG =25) were diagnosed with Major Depressive Disorder, and showed the PSQI score above 5. **Average age**: 33 years, range = 21-51 **Exclusion criteria**: not specified	**Method**: Listening to music **Genre of music:** The 45-minute flute-based compositions were based on the Indian classical music: raags Bahar, Bihag, Mishra Pilu and Malay Martutam. These were recorded on the cassettes. **Setting:** The participants listened to the cassettes and instructed to lay in bed in a quiet environment, beginning an hour prior to their normal bedtime for four weeks. They were also monitored for their adherence to the protocol including the manner of using the cassettes and their ongoing medications, antidepressant and/or sedative. (Frequency: 45 min. every night for 4 weeks) **Compared intervention:** Control group received the standard care with hypnotic medication (mean dose of Diazepam= 7 mg and Chlordiazepoxide= 10 mg).	**Primary**: Pittsburgh Sleep Quality Index (PSQI) **Secondary:** Montgomery Asberge Depression Rating Scale (MADRS)	Insomnia (combined with the certain depression disease.)

Study	Participants	Interventions	Outcomes	Notes
Harmat et al. [74] Method: RCT, three- arm study design (music vs. audiobook vs. control group)	94 participants (Music group = 35; Audiobook group = 30; Control group = 29) were able to understand the Hungarian language, having poor sleep assessed by Pittsburg Sleep Quality Index (global score >5), having no daytime somnolence assessed by Epworth Sleepiness Scale (score <16), and having no severe depressive symptoms assessed by Beck Depression Inventory (score <19). **Average age** (Mean±SD): 22.6±2.83 (range: 19–28) **Exclusion criteria**: (1) current use of hypnotics, sedatives or antidepressants; and (2) medical diagnosis for primary sleep disorder.	**Method**: Listening to music **Genre of music:** The music was a collection of relaxing classical music including some popular pieces from Baroque to Romantic. **Setting:** The music was the same for all participants. The music collection was introduced to the participants by the investigators before the study and they listened at home. Each music excerpt lasted 3 minutes. (Frequency: 45 min. every night at bedtime for 3 consecutive weeks.) **Compared intervention(s)**: (1) The audiobook group were given a CD containing 11 hours of short stories by Hungarian writers. They were asked to listen at bedtime for 45 minutes each night for 3 weeks. (2) The control group received standard care.	**Primary**: PSQI **Secondary**: (a) Beck Depression Inventory (BDI) for measuring mood and depression. (b) The Epworth Sleepiness Scale (ESS) for accessing daytime somnolence.	Insomnia (unspecified combination with a particular diagnosis or other clinical condition)
Hu et al. [91] Method: RCT	45 participants (IG = 20, CG = 25) after cardiac surgery stayed 2 nights in ICU, having neither history of diabetes nor of neurological disorders, being able to communicate and understand the sleep questionnaires, having Glasgow coma score >10 in the first and second day of residence. **Average age** (Mean±SD): 56.7±11 **Exclusion criteria**: (1) severe sleep disorder before surgery; (2) with postoperative complications, renal failure, unconsciousness, coma; (3) requiring sedation and analgesics.	**Method**: Listening to music **Genre of music:** Sounds of nature and animals, and classical music, including Blue Danube, Moonlight Sonata, Morning Song, Lofty Mountains and Flowing Water, Clouds Chasing the Moon etc... **Setting:** Musical pieces were recorded on an MP3 player. Sound of nature was played in the morning, and sound of animals (e.g. fogs and waves) in the evening. Classical music was provided as an aid of relaxation before bedtime for 30 minutes. In addition, the earplugs and eye masks were retained during sleep. **Compared intervention:** standard care	**Primary**: Richards-Campbell Sleep Questionnaire (RCSQ) **Secondary:** Nocturnal melatonin and cortisol levels in urine	Sleep disturbances in ICU
Kong et al. [121] Method: RCT	164 adults (IG= 80, CG= 84) with poor sleep (Pittsburg Sleep Quality Index (PSQI), score >7) **Average age** (Mean±SD): 38.63±7.83 **Exclusion criteria**: People with major physical and neurological disorders	**Method**: Vibroacoustic therapy (VAT), a kind of receptive music intervention. **Genre of music:** Vibra-music with "Gong" tonality **Setting**: Participants received the sleep health education and then sat on the special equipment, like a deck chair. Through this equipment, the low frequency of music was converted into physical vibration working on the human body. Thus, people felt the sound wave during listening music. (Frequency: 40 min. 5 times/ week. Total treatment= 2 weeks) **Compared intervention:** Sleep health education	**Primary**: PSQI **Secondary:** Symptom checklist 90 (SCL-90)	Insomnia (unspecified combination with a particular diagnosis or other clinical conditions)

Study	Participants	Interventions	Outcomes	Notes
Kullich et al. [115] Method: RCT	65 patients (CG= 33, IG=32) suffered from painful Spinal syndrome. (N=46 with chronic low back pain; N=19 with chronic lumbar syndrome) **Average age:** 48.37 (range=21-68) **Exclusion criteria**: (1) hearing impairment; (2) suffering from Tinnitus, Epilepsy; (3) having alcohol abuse or drug abuse; (4) taking any medication or receiving psychological treatment; (5) under aged 18	**Method**: Listening to music and relaxation instructions with a standardized physiotherapy **Genre of music:** Music CD ,,Entspannung bei Schmerzen", Mentalis Verlag, ISBN: 3-932239-95-4. **Setting:** Patients listened music with the earphone in a comfortable, silent place. (Frequency: At least once per day, 25 min. per unit time, for 3 weeks) **Surrounding elements:** not specified **Compared intervention:** Control group received a standardized physiotherapy.	**Primary**: PSQI **Secondary:** (a) VAS for rating pain syndrome. (b) Roland-Morris Disability Questionnaire (RMDQ)	Insomnia (combined with Low-back-pain disorder)
Lafci et al. [78] Method: RCT	60 patients (CG= 30, IG= 30) with breast cancer complained poor sleep (PSQI > 5); staying in hospital at least for a week; and being able to communicate. 56.7% of patients in CG had a cancer diagnosis for over one year, so did in IG. **Average age** (Mean±SD): 48.8±2.4 (range= 27-69) **Exclusion criteria**: (1) having auditory or speech problem; (2) being drug; (3) having psychiatric disorder (e.g. Alzheimer, Parkinson) (4) taking any analgesic and anesthetic medication.	**Method**: Listening to music **Genre of music:** Turkish soft Music (Hicaz and Zirefkend music) **Setting:** A central music system was utilized to play music between 21:00-1:00 every night for seven days. **Surrounding elements:** not specified **Compared intervention**: Control group received an audiobook treatment.	**Primary**: PSQI **Secondary:** VAS for recording satisfaction of patients	Insomnia (combined with cancer)
Lai et al. [76] Method: RCT	60 elderly People (CG= 30, IG= 30) had normal cognitive function; speaking Taiwanese or Chinese; reporting ability to hear radio or TV without a hearing aid; having poor sleep (PSQI >5); not showing sleep apnea on the Epworth Sleepiness Scale (ESS<16); and did not attribute sleep problems to environmental factors, such as mattress, temperature, light, or noise. **Average age** (Mean±SD)**:** 67±5 (range: 60-83) **Exclusion criteria:** People took sleep medicine; having a medical diagnosis of Parkinson's or Alzheimer's disease, having major depressive disorder, asthma, seizures, or a primary sleep disorder, and consuming caffeine within 10 hours before bedtime.	**Method**: Listening to music **Genre of music:** Six types of sedative music contained west synthesizer, harp, piano, orchestra, Jazz music, and Chinese Orchestra. The tempo of the sedative music was 60–80 beats/minute without accented beats, percussive characteristics, or syncopation. **Setting:** At the first home visit, participants were asked to select one preferable type of music and to practice the technique of relaxation. In the following weeks, they listened the selected music und did relaxation at bed time by themselves. (Frequency: 45 min/ per week for 3 weeks). **Surrounding elements:** The investigator gave participants some instructions for relaxation, e.g. sitting back, letting their lips go soft. The selected Music was replayed at a comfortable volume**. Compared intervention:** Control group received no treatment.	**Primary**: PSQI	Insomnia (unspecified combination with a particular diagnosis or other clinical conditions)

Study	Participants	Interventions	Outcomes	Notes
Lee and Kim [90] **Method: RCT**	58 breast cancer patients* undergoing chemotherapy, aged 30-50, staying in the hospital. ** More details about this study was not provide, because the whole text was written in Korean*	**Method**: Listening to music **Genre of music:** Music was selected according to patient's preference. **Setting:** The chosen music was provided twice a week, 30 minutes of each session. There were total eight sessions. **Compared intervention:** standard care	**Primary**: Verran & Snyder-Halpern sleep scale questionnaire (VSH) **Secondary:** Depression Scale (SDS)	Insomnia (combined with cancer)
Liu et al. [122] **Method: RCT**	121 Taiwanese pregnant women with poor sleep (PSQI >5), at 18-34 weeks of gestation. 128 women were initially assigned randomly. Seven women withdrew from the follow-up.	**Method**: Listening to music **Genre of music:** symphonic music arranged on the base of Taiwan songs), western classical music (Beethoven: Für Elise; Debussy: Preludes), nature sounds, lullabies (Brahmus, little star)… **Setting:** Five prerecorded CDs were provided for selection of music. Each CD consisted of different music pieces for 30 minutes. The tempo of music was controlled in a rate of 60-80 beats per minute as similar to the human heart rate. Music was conducted daily at bed time for two weeks. **Compared intervention:** standard care	**Primary**: PSQI **Secondary:** State-Anxiety Inventory (S-STAI) Perceived Stress Scale (PSS)	Insomnia (combined with pregnancy)
Ma et al. [71] **Method: RCT**	200 preoperative patients (CG= 100, IG= 100) were still conscious and recruited from have hepatic surgery, Urology, Orthopedics, or Gynecology; receiving local anesthesia. **Average age:** 39.5 (range: 16-60) **Exclusion criteria**: (1) Patients received general anesthesia; (2) having the history of mental disorder; (3) suffering from Insomnia for long time, and (4) having severe heart or lung disease.	**Method**: Listening to music with sleep hygiene information. **Genre of music**: Sedative music style **Setting:** Before listening, participants were instructed by caregiver to empty their bladders and position themselves comfortably. Then, listening to music with the breathing exercise was conducted with earphone. **Compared intervention**: Standard care with sleep hygiene information	**Primary**: Self-Rating Anxiety Scale (SAS)	Surgery-related sleep disturbance
Mottaghi et al. [75] **Method: RCT, three-arm study design (music vs. cognitive behavioral therapy vs. control)**	61 seniors over 60 years (music=22; CBT=19, control=20) with primary Insomnia disorder (PSQI>5), being a member of Shiraz adult day center, willing to participate, smoking less than 10 string a day. **Average age** (Mean±SD)**:** 68.08±6.18. **Exlusion criteria:** Seniors having secondary sleep disorder, such as medical problems that leaded to insomnia; and having unwillingness to follow the treatments; or being no possible to follow up.	**Method**: Listening to music **Genre of music:** The sedative music and energetic music were provided. **Setting**: Music was performed through prerecorded CD containing the sedative music for bedtime, which was used for 45 minutes, and the energetic music, which was played in the morning for enlivening patients. The intervention was conducted twice per day for four weeks. **Compared intervention(s):** One group received cognitive behavioral therapy (CBT) and the other group had no treatment.	**Primary**: PSQI	Insomnia (unspecified combination with a particular diagnosis or other clinical conditions)

Study	Participants	Interventions	Outcomes	Notes
Neal et al. [96] Method: RCT	41 preterm Infants (CG= 20, IG= 21); born in 32 to 35 weeks gestational-age, being 3 to 10 days of age, having APGAR for 5 minute with score of 8 -10, Passing hearing test, and being clinically stable. **Exclusion criteria**: 1) Diagnosis of congenital defects, IVH, NEC, PDA, sepsis, acute lung disease, or neonatal anemia (Hgb <12 gm/dL), and infant's mothers had 2) had current ventilator use, 3) known maternal drug, alcohol, or illegal substance absue, 4) currently receiving medications for sedation, and 5) current overhead phototherapy abuse.	**Method**: Listening to music **Genre of music:** Brahms' Lullaby was played on a piano with 60 beats per minute. The pitch range of this piece was an octave from the B (494 Hz) in the treble clef to the B above it (987 Hz). This piece has soothing, stable, and unchanging sounds to reduce alerting responses as well as light rhythmic emphasis and a constant rhythm. **Setting of Intervention:** After equipment was set up, pulse oximeter and video camera recording was initiated. The music or ambient noise sound was started after 10 minutes and stopped after 20 minutes. The video camera and pulse oximeter recordings continued until 10 minutes after sound recording was stopped. **Compared intervention**: recorded ambient noise with standard NICU care.	**Primary:** Infant behavioral state **Secondary:** Oxygen saturation heart rate	Sleep development in preterm-infants
Neander et al. [94] Method: RCT	197 participants (CG= 113, IG= 84) had received Hip replacement surgery. **Exclusion criteria:** not specified **Average age:** CG: 74.3 years, range=55-81 IG: 68.3 years, range=54-73	**Method**: Listening to music **Genre of music:** "Low Swin", a quiet music style for improvisation, was played, which reflected an image of the wide ocean ("Voices of the sea"). Besides, "Paul Winter Consort", an orchestra music with wind instruments, guitar and percussion, was also used. **Setting:** Music was added for the first 7 days after surgery and was played for twice a day. Earphone was provided. **Compared intervention:** Patients in the control group took sleeping pill according to their need.	**Primary:** Sleep EEG **Secondary:** **(**a) EOG (b) Electrical resistance of the skin (c) VAS for pain intensity (d) HLM-Monitoring (Hand- & Fußgelenk- Aktigraphen)	Surgery-related sleep disturbance
Olischar et al. [49] Method: RCT	Healthy Preterm Infants (CG= 10, IG= 10) born≥32 weeks' gestational age; requiring investigation or specialist consultation for a non-neurological condition; and less than six weeks of postnatal age. **Exclusion criteria:** not specified **Gestational age:** IG: Median=33.7, range: 33+2-41+2 CG: Median=38.1, range: 36+0-42+0	**Method**: Listening to music **Genre of music:** Brahms' Lullaby from the Australian produced Music for Dreaming was selected.Lullaby melody has more descending contours, fewer contour changes, steady tempos. **Setting** : The music was presented after the first SWC on aEEG for approximately 20 min. **Surrounding elements:** Music was administered to the infants using a Sony Discman and speakers arranged at 30 cm from the infant's head. Sound levels presented around 50–55 dB. **Compared intervention**: The control group was monitored by aEEG without musical stimulation.	**Primary:** aEEG was used to record sleep-wake cycles (SWC) **Secondary:** Prechtl's method behavioural state	Sleep development in preterm-infants

Study	Participants	Interventions	Outcomes	Notes
Puhan et al. [95] Method: RCT	25 participants (CG=11, IG=14) were aged > 18 years with self-reported snoring and an apnea-hypopnea index of 15-30. **Average age:** IG=49.9, CG=47.0 **Exclusion criteria:** Participants (1) received current CPAP therapy; (2) having use of central nervous acting drugs (such as benzodiazepines); (3) currently planning intervention for weight reduction; (4) having consumption of ≥ 14 alcoholic drinks a week or ≥ 2 a day, and (5) obesity (body mass index (kg/m2) ≥ 30).	**Method**: Didgeridoo playing **Instrument:** A standardized acrylic didgeridoo that costs 80 Euro. The didgeridoo is 130 cm long with a diameter of 4 cm and an elliptical embouchure with a diameter of 2.8-3.2 mm. **Setting:** The instructor gave the first individual didgeridoo lesson immediately after randomization. Participants learnt the lip technique to produce and hold the keynote for 20-30 seconds. In the second lesson (week 2) the instructor explained the concept and technique of circular breathing. In the third lesson (week 4) the instructor taught participants how to further practice lips, the vocal tract, and circular breathing. In the fourth lesson, eight weeks, the instructor and the participants repeated the basics of didgeridoo playing. **Frequency:** Participants practiced at home for at least 20 minutes on at least five days a week and recorded the practicing date and time for 4 months. **Compared intervention:** Control group was those people remaining on a waiting list and would start their didgeridoo training after four months.	**Primary:** PSQI **Secondary:** (a) Epworth Sleepness Scale(ESS) (b) A partner's rating for sleep disturbance; (c) German SF-36 (d) Apnoea-Hypopnoea index (AHI)	Breathing - related sleep problem
Reinhardt et al. [44] Method: RCT	28 patients (CG=14, IG=14) with chronic cancer pain in a stable phase of the disease, without rapid progressive disease. **Average age**: Range: 36-74 **Exclusion criteria:** Patients with Fever, Anemia or cardiopulmonary disease.	**Method**: Listening to music with a relaxation program **Genre of music:** Music was performed by a chamber orchestra included synthesizer and Messo-sopran. It was a lullaby-like music style. **Setting**: The patients in IG listened the music tape for 13 nights at bedtime. The tape of relaxing music «Ein Weg in den Schlaf» (Edel Records 0001572CCC, Eterna 729195) was used, which consisted of a 30 min. relaxation and vocal-instrumental music. A speaker-aside led a "fantasy jouney" arranged by Arno Holtz (Holz, Arno: Phantasus. 1. Heft. Berlin, 1898. In: Deutsches Textarchiv) (Frequency: 30 min. per day, at bedtime, for 13 nights). **Surrounding elements:** This lullaby-like music has 6/8- beat at a tempo of 56-58 bpm (beat per minute). With a continuing ritardando it became 44 bpm after 10 min. and 36 bpm after 20 min. **Compared intervention**: The control group was not exposed to music relaxation program.	**Primary:** Level of synchronization between heart rate and musical rhythm **Secondary:** (a) 6-level Verbal Rating Scale (VRS) for assessing pain (b) VRS for assessing relaxation degree (c) Daily log for recording whether or not falling asleep and	Sleep problem associated with cancer pain (The relative diagnosis of insomnia was not made in this study)

Study	Participants	Interventions	Outcomes	Notes
Renzi et al. [92] Method: RCT	86 patients (CG=43, IG=43) were undergoing surgery for benign anorectal diseases. **Exclusion criteria:** not specified **Average age:** IG: 48 years, range: 25-7 CG:44 years range: 18-70	**Method**: Listening to music with a relaxation program **Genre of music:** The use of relaxation techniques “guided imaging” (GI) consisted of a soft, “new-age-lke” musical in the background and a relaxing text. **Setting:** The patients were encouraged to listen to the tape once 1 h before entering the operating room, once or twice during surgery depending on the duration of the operation, and at least twice within 48 h after surgery before discharge. (Frequency: 30 min. music tape was used 1 h before, during, and after surgery) **Compared intervention:** The control group received a standard treatment.	**Primary:** VAS: 1=quiet sleep; 10=insomnia**.** **Secondary:** (a) VAS for postoperative pain (2) The nature of first micturition was determined as either normal or difficult.	Surgery-related sleep disturbance
Richards et al. [62] Method: RCT, three-arm study design (music vs. back massage vs. control)	69 male (music relaxation=28, back massage=24, usual nursing care=17); having diagnosis of cardiovascular illness, being able to read, speak and hear conversational English; staying in stable hemodynamic status (a systolic blood pressure greater than 90mm Hg, a diastolic blood pressure less than 120mm Hg…), and being hospitalized in the Coronary Care Unit (CCU) for no more than 48 hours before selection for the study. **Average age:** 65.8 years, range=55-79 **Exclusion criteria**: Patients had prior diagnosis of obstructive sleep apnea.	**Method**: Listening to music with a relaxation program **Genre of music:** The music relaxation program consists of progressive muscle relaxation, mental imagery and background music. The music was Water Spirit from the album Water Spirit by Kim Robertson. **Setting:** All patients’ rooms were single units. Each room had a bedside monitor, a thermostat for regulating room temperature. A 7.5 min. audiotape played with comfort sound level at bedtime for one night. Headphone was used by listening. **Compared intervention(s):** the back-massage group received a 6-minute massage, and the control group received the routine nursing care (plus 6 min rest period).	**Primary:** PSG (16 Channel EEG machine was used. ECG, EOG and EMG data were recorded. Sleep was measured with 2 channels of central and occipital, 1 chin EMG channel, 2 EOG channels.)	Sleep disturbance in CCU
Ryu et al. [1] Method: RCT	58 subjects (CG=29, IG=29) were ≥20 years old, having diagnosis of coronary artery disease, being admitted to CCU after PTCA (Percutaneous Transluminal Coronary Angioplasty) **Average age:** 61.2 years **Exclusion criteria:** Subjects used ventilators, being diagnosed of dementia, neurologic disease, or sensory disorder, taking sleep-inducing drugs or sedative medications, and having history of sleeping problem before admittance to CCU.	**Method**: Listening to music **Genre of music:** Sleep-inducing music was performed with low volume, which stimulated higher levels of Delta-wave brain pattern of sleep. Alpha-waves, which are antagonistic to sleep, are lessened. This music included Nature Sounds (2.80’), Delta Wave Control Music (5.21’), Goldberg variations BWV. 988 (27.3’), Nature Sounds (4.57’), Goldberg Variations (11.10’) and Nature Sounds (2.25’). **Setting:** Through the earplug, sleep-inducing music was delivered for 52 min. began at 10:00 PM. When a subject fall asleep, the earphone was intentionally not removed until 5 AM. the next morning. **Compared intervention:** Eye shield and earplugs were provided from 10 PM–5 AM the next morning.	**Primary:** (a) VSH sleeping scale. (b) Log for time of falling asleep and of awakening time	Sleep disturbance in CCU

Study	Participants	Interventions	Outcomes	Notes
Schlez et al. [72] Method: RCT; a within-subject, crossover, repeated design	52 stable preterm-infants born between 32 and 37 weeks of gestation, and having normal hearing confirmed by measurement of distortion product otoacoustical emission. 52 Mothers having ability to hear, read, answering an anxiety questionnaire, and having no signs or medical history of postpartum depression. **Gestational age:** 32 weeks, range=26-36 **Mothers' average age: 3**0 years, range: 19-46 **Exclusion criteria:** Preterm-babies: (a)having hyper-responsiveness to live music therapy, as opposed to other sounds, and defined as crying when music starts and relaxing when music stops; b) congenital anomaly that mainly affects hearing, such as craniofacial anomalies; c) medication intake such as phenobarbital…, which might interfere with the reaction to musical stimuli; and d) brain anomalies associated with neurological disorders.	**Method**: Listening to music with kangraroo care **Genre of music:** Live harp music was performed by a single experienced musician. A blend of Eastern and Western melody was chosen, which was simply improvised in the style of lullabies with soothing and repetitive wordless melodic lines. The 60-70 beats per minute, matching the resting adult heartbeat, were applied. **Setting:** Music was played at a distance of 1 to 2 meters from the infant-mother dyad. The mothers were sitting at the infants' bedside in the feed-and-grow area that serves stable preterm infants. The infant was placed in the kangaroo position, assuring skin-to-skin contact with the mother. Each therapy session began 30 minutes after feeding to ensure, that infants had no hunger. **Surrounding elements:** The mean sound level in the pre-study was recommended (50-65 dB). And the ambient noise was controlled at the lowest possible level, approximately 40 dB. **Compared intervention:** Kangraroo care alone	**Primary:** A 7-point scale to assess infants' behavioral state **Secondary:** (a) State-Trait Anxiety Inventory (STAI) for measuring maternal anxiety symptoms (b) Neonatal and maternal heart rates, (c) Oxygen saturation levels (d) Respiratory rates were recorded every 2 minutes during all sessions.	Sleep development in preterm-infants
Su et al. [93] Method: RCT	28 patients (CG=14, IG=14), 1) age>18 years old; (2) Acute Physiology and Chronic Health Evaluation, (APACHE II) score _25 (Chao 1995); (3) ability to communicate in either Mandarin or Taiwanese; (4) being conscious and clear; (5) having a length of residency in the ICU of more than 24 hours; (6) having an arterial catheter inserted. **Average age** (Mean±SD)**:** 61.68 ±9.82 (range: 39-78) **Exclusion criteria:** (1) hearing impairment; (2) physical restraint; (3) alcoholism; (4) infectious disease; (5) haemodynamic instability.	**Method**: Listening to music with a relaxation program **Genre of music:** The chosen 4 musical pieces were composed of sedating piano music. All of them had similar characteristics, including a smooth rhythm to achieve a relaxing effect, a tempo of 60–80 beats/min, minor tonalities, smooth melody lines and no dramatic changes in volume and rhythm. **Setting of Intervention:** Participants listened to music for 45 min. at nocturnal sleep time. The music was played on a Sony (CFD-S07CP) CD player (Japan). The participants were told to let the music continuously play and not to worry about turning it off. **Surrounding elements:** The music volume was set at a comfortable level for participants; between 30–40 dB according to the World Health Organization guidelines for sound levels in hospitals during the night. All participants slept in a dim, temperature and light-controlled single room. Lights-out was initiated after the preparation of the electrode montage. The room temperature ranged between 21–23°C. **Compared intervention(s):** Standard treatment	**Primary:** (a) VSH Sleep scale (b) PSG **Secondary:** (a) heart rate, (b) mean arterial; (c) Blood pressure; (d) Respiratory rate; (e) APACHE II (Acute Physiology and Chronic Health Evaluation II)	Sleep disturbance in CCU

Study	Participants	Interventions	Outcomes	Notes
Shum et al. [77] Method: RCT	60 elderly people (CG= 30, IG= 30) aged above 55 years; able to speak English or Mandarin; living in Singapore; being physically capable of completing assessment; having poor sleep (PSQI >6). **Average age** (Mean±SD)**: 6**4±8.0 (range: 57-68.8) **Exclusion criteria:** People with abnormal cognitive function, such as Parkinson's disease or dementia; having hearing difficulties.	**Method**: Listening to music **Genre of music:** Soft, instrumental slow sedative music without lyrics, including Western classic (Bach, Mozart, Chopin etc…), Chinese classic, and Jazz (Everlasting, Winter Wonderland etc…) **Setting:** Participants were provided with an MP4 player with earphones and listened to the music of their choice from a prerecorded music-selection for 40 minutes. They were required to use a single genre of music within the same week. Music Intervention was conducted for six weekly visits, once a week. In addition, the participants were reminded to listen music once a day. **Compared intervention:** The control group only took an uninterrupted rest during the visit of researcher**.**	**Primary:** PSQI	Insomnia (unspecified combination with a particular diagnosis or other clinical conditions)
Suwansathit et al. [123] Method: RCT	140 subjects (CG= 70, IG= 70) stayed in sleep center in Bangkok, Thailand. (*It was a conference abstract providing only few details.)	**Method**: Listening to music **Genre of music:** 30 minutes of Tail light music **Compared intervention:** standard care	**Primary:** PSG **Secondary:** STAI	Insomnia (unspecified)
Wang et al. [51] Method: RCT	64 elderly people (CG= 32, IG= 32) aged above 60 years with poor sleep (PSQI >7); able to communicate in Chinese. **Average age** (Mean±SD**):** 69.38±5.46 **Exclusion criteria:** People with cognitive disabilities; having hearing difficulties; having a history of drug or alcohol abuse.	**Method**: Listening to music **Genre of music:** 169 music pieces were collected in a music database and recorded in the MP3 player Music styles included Chinese instrumental classic, Western classic, nature sounds, classical songs without lyric. Most of them were soft and played with stable melodies and tempo of 60-80 beats per minute. **Setting:** The Participants selected the preferred music from the music database and listened for 30-45 minutes per night before sleep for three months. **Compared intervention:** No music provided	**Primary:** PSQI	Insomnia (unspecified combination with a particular diagnosis or other clinical conditions)

Study	Participants	Interventions	Outcomes	Notes
Wepner et al. [41] Method: RCT three-arm study design (music vs. placebo vs. control)	54 patients aged 20-60 with unspecific spinal pain (>3 months), e.g. Lumbago pain, spinal pain, back pain. **Average age** (Mean±SD**):** 47.06±9.329, range=29-60 **Exclusion criteria:** Patients with extreme degenerative changes to lumbar spinal column, Meyerding strage3, motor-sensory deficits, infection conjunctivitis, malignant tumors or post-spinal-operation. *Sample size in each group was not reported.	**Method**: Crystal singing bowls, a kind of receptive music therapy **Instrument:** Crystal Singing Bowls (German: Klangschalentherapie) **Setting**: Patients chose one of three singing-bowls (with sound a, f' or g'). Therapist lay it on different body regions of patients, e.g. on the belly, back or foot. The singing-bowl was moved upward and downwards on patient's back, especially on the painful region of body. (Frequency: 30 min. 4 weeks for total 6 treatment units) **Compared intervention(s):** Similar to the intervention group, patients in placebo group chose a singing-bowl as well. But the bowl was not played and did not work on the painful region of body. The control group (ZG) received standard care.	**Primary:** ECG for documenting heart rate, the sleep phases, and sleep time **Secondary:** (a) Electrical skin conductance (b) Roland-Morris Disability Questionnaire (c) SF36 (d) Multidimensional Mood State (MDBF) Questionnaire (e) VAS for pain	Insomnia (combined with pain disorders)
Zimmerman et al. [40] Method: RCT	96 Postoperative CABG Patients (Coronary Artery Bypass Graft) (Music group=32, Music video=32 vs. CG=32)); able to speak and read English; over 19 years old; extubated within 24 hours postoperatively, and removal of intra-aortic balloon pump within 12 hours postoperatively. **Average age** (Mean±SD**):** 67±9.9, range:37-84 **Exclusion criteria:** People having hearing deficit	**Method**: (a) Listening to music; (b) Listening to music with visual image **Music along:** Participants selected one from 5 prerecorded audio tapes with soothing style, including (1) Country Western Instrumental by Country Pops; (2)Fresh Aire by Mannheim Steamroller; (3)Winter into Spring by George Winston; (4) Prelude, and (5) Comfort Zone by Steven Halpern. **Music video*:*** A 30-minute videocassette with soft instrumental music and visual images was played, including three options: (1) Water's Path; (2)Western Light; or (3)Winter by Pioneer Artis. (Length of intervention: 30 min.) **Compared intervention(s):** Participants had 30-minute rest period but were not exposed to any music.	**Primary:** Richards-Campbell Sleep Questionnaire (RCSQ) Secondary: (a) VRS (b) MPQ (MeGill Pain Questionnaire)	Surgery-related sleep disturbance

Appendix D: Excluded studies / Ongoing studies

Study	Reason for exclusion
Chan et al. [110]	Duplication of Chan 2010
Dorn et al. [124]	No RCT
Lai et al. [125]	Cross-over design without wash-out
DuRousseau [126]	No RCT
Field et al. [65]	Music was one of multiple components used in the intervention group. Therefore, the effect of music could not be evaluated separately. No sleep-related outcome assessment was found.
Gitanjali et al. [127]	All groups received music intervention. This study was to compare different kinds of music intervention.
Good et al. [116]	The score of sleep quality was not porvided seperatly in IG and CG.
Hughes et al. [106]	no matching intervention
Jacobs et al. [128]	This study recruited people without sleep problems.
Lai	This dissertation is not available after contacting the first author. But this study has been published in a journal article. See Lai et al. [76]
Lai et al.	See Lai et al.[76]
Lai et al. [129]	No matching intervention
Lazic et al. [130]	No RCT
Loewy et al. [131]	The study design did not match the criterion.
Modugno et al. [132]	The outcome concerning level of daytime drowsiness was not matched.
Smith et al. [133]	Music was used to improve the adherence to CPAP treatment. It didn't relate to sleeping problem.
Street et al. [134]	No RCT
Tan et al. [135]	The studied objects are healthy children, which didn't match the inclusion criterien.
Conference proceedings	
Dehkhoda et al. [136]	Conference proceeding. No more details were provided in the given abstract.
Haimov et al. [137]	Conference proceeding. No more details were provided in the given abstract.
Haimov et al. [138]	Conference proceeding. No more details were provided in the given abstract.
Kayumov et al. [139]	Conference proceeding. No more details were provided in the given abstract.
Lai et al.	Conference proceeding. Only the abstract available. But the result has been published. See Lai [76]
Liu et al. [122]	Conference proceeding. No more details were provided in the given abstract.
Liu et al. [140]	Conference proceeding. No more details were provided in the given abstract
Lv et al. [141]	Conference proceeding. No more details were provided in the given abstract.
Sithinamsuwan et al. [142]	Conference proceeding. the first author was contacted, but more details were not provided.
Tang et al. [143]	Conference proceeding. the first author was contacted, but more details were not provided.
Tsai et al. [144]	Conference proceeding. No more details were provided in the given abstract.
Ongoing studies / studies awaiting assessment [ordered by ClinicalTrials.gov identifier]	
NCT02376686	Music Intervention in the Treatment of Sleep Disorders for Depressed Patients
NCT02493348	A Study of the Effect of Rhythmic Sensory Stimulation and Music on Fibromyalgia
NCT02394938	Effects of Recorded Music in Heart Failure Patients (EMSC)

Appendix E: Treatment of missing data and data conversion

Outcomes	Study ID	Handling with missing data	Converting from the given data		
Pittsburgh Sleep Quality Index (PSQI)	Kullich et al. [115]	The SD of control group was missing and could not be calculated, because only the change score was reported. But this missing value had been obtained by the other review author (de Niet, 2009). Through this review article, the missing value was documented. **(See note 1 & 2 blow)**			
Verran & Snyder-Halpern sleep scale (VSH)	Lee and Kim [90]	VSH preforms the different direction of evaluation, and thus must be converted by maximum score – real score. The SD remained as the same. (**See note 3 blow)**		IG (Mean±SD)	CG (Mean±SD)
			Original	36.14±2.05	=24.24±1.09
			converting of mean (max.–real score)	80-36.14=43.86	80-24.24=55.76
			converted score	**43.86±2.05**	**55.76±1.09**
	Ryu et al. [1]	VSH preforms the different direction of evaluation, and thus must be converted by maximum score – real score. The SD remained as the same. . (**See note 4 blow)**		IG (Mean±SD)	CG (Mean±SD)
			Original	36.14±5.68	29.41(3.85)
			converting of mean (max.–real score)	80-36.14=43.86	80-29.14=50.59
			converted score	**43.86±5.68**	**50.59±3.85**
	Su et al. [145]	VSH preforms the different direction of evaluation, and thus must be converted by maximum score – real score. In this study, SD was not provided, because the generalized estimating equation was used for estimating the variances presenting between different measuring time. Accordantly, the estimated value was not merely the traditional "mean value" anymore, but the average response of participants in each group after evaluation of unknown correlation. Meanwhile SE were modified to be more robust. Then, SD was predicted by standard error. The number in intervention and control groups was 14, respectively.		IG (Estimate; SE)	CG (Estimate; SE)
			Original	545; 11.20	497; 15.17
			converting of SD [SD=SE*sqrt(N)]	11.20*sqrt (14) =41	15.17*sqrt (14) =56
			converting of mean (max.–real score)	1500-545=955	1500-497=1003
			converted score Estimate; SD	**955; 41**	**1003; 56**
Richard Sleep Questionnaire (RSQ)	Zimmerman et al. [40]	RSQ scores must be converted by maximum score – real score, due to the different direction of evaluation. The SD remained as the same.		IG (Mean±SD)	CG (Mean±SD)
			Original	6.8±2.45	5.63±2.43
			converting of mean (max.–real score)	10-6.8=3.2	10-5.63=4.37
			converted score	**3.2±2.45**	**4.37±2.43**

Richards-Campbell sleep questionnaire (RCSQ)	Hu et al. [91]	RCSQ (Chinese version) contains the same direction of evaluation as PSQI. A value of null means good sleep. There was no need to convert. The total score was obtained from 6 items (subscales); each of them contained a 100-mm visual-analog scale (VAS). This study was only provided the mean and SD of each separate item, not the total score. Therefore, one of the 6 items - perceived quality – was chosen for analysis.
Self-Rating Anxiety Scale (SAS)	Ma et al. [71]	Ordinal data was transformed to dichotomous (%)

Note:

1) **Some abbreviations: SD = standard deviation, SE = standard error, IG = intervention group, CG = control group, sqrt = square root**
2) **Most of studies used the Pittsburgh sleep quality index questionnaire (PSQI) for measuring sleep quality. Therefore, the direction of valuation of PSQI was taken as the standard direction: the lower the score, the better the quality of sleep.**
3) **The VSH used in the studies of Lee et al. [90] and Ryu et al. [1] was a modified version. It included eight questions regarding the frequencies of awakening while sleeping, depth of sleep and self-evaluation of sleep. A Likert scale ranged from 0–10 for each question has a total possible score that ranges to 80.**
4) **The VSH in Su' study [145] consisted of 15 items with visual analogue scale running from 0–100 mm. The sum of the scores provided a global sleep quality score ranging from 0–1500. Lower scores indicated poorer sleep quality.**
5) **See more details in: Liang and Zeger [146]**

Outcomes	**Study ID**	**Handling with missing data**	**Converting from the given data**		
Polysomnography (PSG: Total sleep time= TST)	Chang et al. [118]	The generalized estimating equation was used to control variances between pre- and posttest. As to the previous handling in Su 2013, the estimated value was considered as a modified average of people in the group. SE was provided and then converted into SD.		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*384.5; 6.95*	*397.3; 7.40*
			converting of SD [SD=SE*sqrt(N)]	6.95*sqrt(25)=34.75	7.40*sqrt(25)=37
			converted score (Estimate; SD)	**384.5; 34.75**	**397.3; 37**
	Su et al. [145]	As mentioned in Chang 2012, the estimated value was taken as a modified average of people in each group. SE was provided and then converted into SD.		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*51.25; 2.91*	*49.66; 3.86*
			converting of SD [SD=SE*sqrt(N)]	2.91*sqrt(14)=10.88	3.86*sqrt(14)=14.44
			converted score (Estimate; SD)	**51.25; 10.88)**	**49.66; 14.44)**

Polysomnography (PSG: Sleep efficiency; total sleep time/total recording time =SE)	Chang et al. [118]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*92.9; 0.79,*	*93.07; 0.88*
			converting of SD [SD=SE*sqrt(N)]	0.79*sqrt(25)=3.95	0.88*sqrt(25)=4.4
			converted score (Estimate; SD)	**92.9; 3.95**	**93.07; 4.4**
	Su et al. [145]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*42.66; 2.41*	*40.62; 3.25*
			converting of SD [SD=SE*sqrt(N)]	2.41*sqrt(14)=9.017	3.25*sqrt(14)=12.16
			converted score (Estimate; SD)	**42.66; 9.017**	**40.62; 12.16**
Polysomnography (PSG: Sleep onset latency=SOL)	Chang et al. [118]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*14.03; 3.14*	*11.41; 1.95*
			converting to SD [SD=SE*sqrt(N)]	3.14*sqrt(25)=15.7	1.95*sqrt(25)=4.4
			converted score (Estimate; SD)	**14.03; 15.7**	**11.41; 9.75**
	Su et al. [145]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*34.39; 3.11*	*49.66; 3.86*
			converting to SD [SD=SE*sqrt(N)]	3.11*sqrt(14)=11.63	3.86*sqrt(14)=14.44
			converted score (Estimate; SD)	**34.39; 11.63**	**49.66; 14.44**
Polysomnography (PSG: Wake after sleep onset=WASO	Chang et al. [118]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*16.59; 2.81*	*19.31; 2.72*
			converting to SD [SD=SE*sqrt(N)]	2.81*sqrt(25)=14.05	2.72*sqrt(25)=13.6
			converted score (Estimate; SD)	**16.59; 14.05**	**19.31; 13.6**
Polysomnography (PSG: % of TST in stage 1)	Chang et al. [118]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*4.7; 0.63*	*6.0; 0.62*
			converting of SD [SD=SE*sqrt(N)]	0.63*sqrt(25)=3.15	0.62*sqrt(25)=3.1
			converted score (Estimate; SD)	**4.7; 3.15**	**6.0; 3.1**
	Su et al. [145]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*17.279; 1.32*	*19.83; 1.93*
			converting of SD [SD=SE*sqrt(N)]	1.318*sqrt(14)=4.93	1.93*sqrt(14)=7.22
			converted score (Estimate; SD)	**17.279; 4.93**	**19.83; 7.22**

Polysomnography (PSG: % of TST in stage 2)	Chang et al. [118]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*49.72; 0.01*	*53.5; 1.45*
			converting of SD [SD=SE*sqrt(N)]	0.01*sqrt(25)=0.05	1.45*sqrt(25)=7.25
			converted score (Estimate; SD)	**49.72; 0.05**	**53.5; 7.25**
	Su et al. [145]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*59.33; 1.72,*	*64.53; 1.24*
			converting of SD [SD=SE*sqrt(N)]	1.72*sqrt(14)=6.435	1.24*sqrt(14)=4.639
			converted score (Estimate; SD)	**59.33; 6.44**	**64.53; 4.64**
Polysomnography (PSG: % of TST in stages 3)	Chang et al. [118]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*18.83; 0.83*	*19.28; 0.79*
			converting of SD [SD=SE*sqrt(N)]	0.83*sqrt(25)=4.15	0.79*sqrt(25)=3.95
			converted score (Estimate; SD)	**18.83; 4.15**	**19.28; 3.95**
	Su et al. [145]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*22.52; 1.78*	*16.04; 1.67*
			converting of SD [SD=SE*sqrt(N)]	1.78*sqrt(14)=6.660	1.67*sqrt(14)=6.248
			converted score (Estimate; SD)	**22.52; 6.66**	**16.04; 6.25**
Polysomnography (PSG: % of TST in REM sleep)	Chang et al. [118]	See above		IG (Estimate; SE)	CG (Estimate; SE)
			Original	*25.0; 0.8*	*22.91; 0.67*
			converting of SD [SD=SE*sqrt(N)]	0.8*sqrt(25)=4.0	0.67*sqrt(25)=3.35
			converted score (Estimate; SD)	**25.0; 4.0**	**22.91; 3.35**

Appendix F: Summary of finding table (GRADE)

Listening to music for adults with insomnia											
№ of participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With standard care/placebo	With music listening		Risk with standard care/placebo	Risk difference with receptive music intervention
Insomnia (unspecified) (assessed with: sleep questionnaires)											
617 (8 RCTs)	serious [a,b]	not serious	not serious	not serious	none	⊕⊕⊕◯ MODERATE	308	309	-	The mean Insomnia (due to unspecified causation) ranged from 5.17-10.07 point	MD 1.44 point fewer (2.6 fewer to 1.4 fewer)
Insomnia due to depression, pain disorders (assessed with: sleep questionnaires)											
109 (2 RCTs)	serious [a,b]	not serious	not serious	Serious [c]	none	⊕⊕◯◯ LOW	54	55	-	The mean insomnia (due to depression, pain disorders) was 8.89 point	MD 1.64 point lower (2.78 lower to 0.51 lower)
Insomnia due to cancer (assessed with: sleep questionnaires)											
118 (2 RCTs)	serious [a,b]	not serious	not serious	serious [c]	none	⊕⊕◯◯ LOW	59	59	-	-	SMD 7.46 SD lower (8.51 lower to 6.41 lower)
Insomnia in elderly people over 60 years (follow up: 3 to 4 weeks; assessed with: sleep questionnaires)											
267 (5 RCTs)	serious [a,b]	serious [d]	not serious	serious [e]	none	⊕◯◯◯ VERY LOW	134	133	-	The mean insomnia in elderly people over the age of 60 ranged from 5.1-9.28 point	MD 1.92 point lower (2.9 lower to 0.93 lower)

Insomnia_treatment duration in 7-14 days (assessed with: sleep questionnaires)										
512 (6 RCTs)	serious [a,b]	not serious [f]	not serious	not serious	none	⊕⊕⊕◯ MODERATE	257	255	-	The mean insomnia in treatment duration 7-14 days ranged from 5.5-10.17 points	MD 1.45 points fewer (2.06 fewer to 0.84 fewer)
Insomnia_treatment duration in 21-30 days (assessed with: sleep questionnaires)										
397 (7 RCTs)	serious [a,b]	not serious [g]	not serious	serious [c]	none	⊕⊕◯◯ LOW	197	200	-	The mean insomnia in treatment duration 21-30 days ranged from 5.17-10.07 points	MD 1.98 points fewer (2.61 fewer to 1.33 fewer)
Total sleep time_insomnia (unspecified) (assessed with: PSG)										
190 (2 RCTs)	serious [a,b]	not serious	not serious	serious [h]	none	⊕⊕◯◯ LOW	95	95	-	The mean TST was 307.85 minute	MD 9.61 minute more (8.15 fewer to 27.37 more)
Sleep efficiency_insomnia (assessed with: PSG)										
190 (2 RCTs)	serious [a,b]	not serious	not serious	serious [h]	none	⊕⊕◯◯ LOW	95	95	-	The mean sleep efficiency was 88.19	MD 0.1 higher (1.98 lower to 2.18 higher)
Sleep onset latency_insomnia (assessed with: PSG)										
226 (3 RCTs)	serious [a,b]	not serious [o]	not serious	serious [h]	none	⊕⊕◯◯ LOW	113	113	-	The mean sleep onset latency was 11.41 minutes	MD 2.62 minutes higher (4.62 lower to 9.86 higher)
Wake after sleep onset_insomnia (assessed with: PSG)										
190 (2 RCTs)	serious [a,b]	not serious	not serious	serious [h]	none	⊕⊕◯◯ LOW	95	95	-	The mean wake after sleep onset was 28.05 minutes	MD 2.72 minutes lower (9.53 lower to 4.1 higher)

NREM stage 1_insomnia (assessed with: PSG)										
190 (2 RCTs)	serious [a,b]	not serious	not serious	serious [h]	none	⊕⊕◯◯ LOW	95	95	-	The mean NREM 1 sleep was 15.5 minutes	MD 1.49 minutes lower (3.14 lower to 0.16 higher)
NREM stage 2_insomnia (assessed with: PSG)										
190 (2 RCTs)	serious [a,b]	serious [i]	not serious	Serious [h]	none	⊕◯◯◯ VERY LOW	95	95	-	The mean NREM 2 sleep was 49.3 minute	MD 0.77 minute lower (7.2 lower to 5.65 higher)
NREM stage 3_insomnia (assessed with: PSG)										
190 (2 RCTs)	serious [a,b]	not serious	not serious	serious [h]	none	⊕⊕◯◯ LOW	95	95	-	The mean NREM 3 sleep was 19.28 minute	MD 0.05 minute lower (2.04 lower to 1.94 higher)
REM sleep_insomnia (assessed with: PSG)										
190 (2 RCTs)	serious [a,b]	serious [j]	not serious	serious [h]	none	⊕◯◯◯ VERY LOW	95	95	-	The mean REM sleep stage was 19.28 minute	MD 3.98 minute higher (0.17 lower to 8.14 higher)

CI: Confidence interval; **SMD:** Standardised mean difference; **MD:** Mean difference

a. There was at least one study without generating random sequence properly or without concealing the allocation adequately. Therefore, the quality of evidence was rated down for one level.
b. Participants receiving music intervention could not be blinded.
c. Although the 95%CI excluded the threshold of null effect, the number of participants was regarded as small (<400).
d. The heterogeneity was detected with MD estimator as moderate level (Tau^2 = 0.61, Chi^2 = 7.69, P = 0.10, I^2 = 48%).
e. The pooled CI was located on the link side of the threshold. Nevertheless, the number of participants was smaller than 400.
f. The heterogeneity among studies was estimated as not important (Tau^2 = 0.16, Chi^2 = 6.84, P = 0.23, I^2 = 27%).
g. The heterogeneity was estimated as not important (Tau^2 = 0.18, Chi^2 = 7.84, P = 0.25, I^2 = 23%). Therefore, the quality of evidence was considered to be downgrade.
h. The 95%CI crossed the threshold of no effect.
i. The heterogeneity was very substantial (Tau^2 = 17.68, Chi^2 = 5.46, P = 0.02, I^2 = 82%).)
j. The heterogeneity among studies was substantial (Tau^2 = 6.41, Chi^2 = 3.19, P = 0.07, I^2 = 69%).

Listening to music for sleep-related epilepsy

№ of participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With standard care	With receptive music intervention		Risk with standard care	Risk difference with receptive music intervention
Sleep quality (assessed with: seizure monitor)											
36 (1 RCT)	serious [a]	not serious	not serious	serious [b]	none	⊕⊕◯◯ LOW	7/11 (63.6%)	5/25 (20.0%)	RR 0.31 (0.13 to 0.77)	636 per 1,000	439 fewer per 1,000 (554 fewer to 146 fewer)

CI: Confidence interval; **RR:** Risk ratio

a. The allocation concealment was not clear.

b. Although the 95%CI excluded the threshold (RR = 1), the prognostic balance might not be assured, due to the small sample size.

Listening to music for premature infants

№ of participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With standard care	With receptive music intervention		Risk with standard care	Risk difference with receptive music intervention
Heart rate											
145 (2 RCTs)	serious [a]	not serious	not serious	serious [b]	none	⊕⊕◯◯ LOW	72	73	-	not pooled	not pooled
O2 saturation											
145 (2 RCTs)	serious [a]	not serious	not serious	serious [b]	none	⊕⊕◯◯ LOW	72	73	-	not pooled	not pooled

CI: Confidence interval; SMD: Standardised mean difference

a. the generation of Random sequence and concealment of allocation were not reported clearly.

b. The effect sizes of studies were not merged due to the diversity of study design. Besides, the number of participants was smaller than 400, which was suggested by Grade handbook for ensuring the prognostic balance.

Listening to music for adults with sleep disturbances in ICU or surgery-related conditions										
№ of participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							standard care	music		Risk with standard care/placebo	Risk difference with receptive music intervention
Sleep disturbance in ICU/CCU (assessed with: sleep questionnaires)											
131 (3 RCTs)	serious [a,b]	not serious	not serious	serious [c]	none	⊕⊕◯◯ LOW	68	63	-	-	SMD 1.23 SD lower (1.61 lower to 0.85 lower)
Sleep disturbance in surgery-related condition (assessed with: sleep questionnaires)											
150 (2 RCTs)	serious [a,b]	not serious	not serious	serious [c]	none	⊕⊕◯◯ LOW	75	75	-	-	SMD 0.53 SD lower (0.85 lower to 0.2 lower)
Total sleep time_sleep disturbance (assessed with: PSG)											
73 (2 RCTs)	serious [a,b]	not serious	not serious	serious [d]	none	⊕⊕◯◯ LOW	31	42	-	The mean total sleep time ranged from 257.33-466.2 minutes	MD 45.98 minutes higher (35.68 higher to 56.29 higher)
Sleep efficiency_sleep disturbance (assessed with: PSG)											
73 (2 RCTs)	serious [a,b]	not serious	not serious	serious [e]	none	⊕⊕◯◯ LOW	31	42	-	The mean sleep efficiency was 49.66 minutes	MD 1.59 minutes higher (7.88 lower to 11.06 higher)
Sleep onset latency_ sleep disturbance (assessed with: PSG)											
73 (2 RCTs)	Serious [a,b]	serious [f]	not serious	serious [d]	none	⊕◯◯◯ VERY LOW	31	42	-	The mean sleep onset latency ranged from 17.84-49.66 minutes	MD 10.45 minutes lower (20.62 lower to 0.27 lower)
Wake after sleep onset_ sleep disturbance (assessed with: PSG)											
45 (1 RCT)	serious [a,b]	not serious	not serious	serious [e]	none	⊕⊕◯◯ LOW	17	28	-	The mean wake after sleep onset was 31.2 minute	MD 5.1 minute lower (17.56 lower to 7.36 higher)
NREM stage 1_ sleep disturbance (assessed with: PSG)											

73 (2 RCTs)	serious [a,b]	not serious	not serious	serious [e]	none	⊕⊕◯◯ LOW	31	42	-	The mean NREM sleep 1 was 18.8 point	MD 1.95 point lower (5.86 lower to 1.95 higher)
NREM stage 2_sleep disturbance (assessed with: PSG)											
73 (2 RCTs)	serious [a,b]	not serious	not serious	serious [g]	none	⊕⊕◯◯ LOW	31	42	-	The mean NREM sleep 2 was 51.1 point	MD 4.36 point lower (8.22 lower to 0.5 lower)
NREM stage 3_sleep disturbance (assessed with: PSG)											
73 (2 RCTs)	serious [a,b]	not serious	not serious	serious [g]	none	⊕⊕◯◯ LOW	31	42	-	The mean NREM sleep 3 ranged from 8.36-16.04	MD 4.94 higher (1.01 higher to 8.86 higher)
REM sleep_sleep disturbance (assessed with: PSG)											
45 (1 RCT)	serious [a,b]	not serious	not serious	serious [e]	none	⊕⊕◯◯ LOW	17	28	-	The mean REM sleep was 3.89	MD 2.94 higher (0.18 lower to 6.06 higher)

CI: Confidence interval; **SMD:** Standardised mean difference; **RR:** Risk ratio; **MD:** Mean difference

a. Random sequence generation and allocation concealment were not clear. Therefore, the quality of evidence was rated down for one level.
b. Participants receiving music intervention could not be blinded.
c. The 95%CI excluded the threshold of null effect. However, the range of CI crossed two levels of effect sizes (medium and large). Thus, the precision of evidence was interpreted as instable.
d. The total 95% CI excluded no effect. The total sample size was relatively small and may led to imprecision.
e. The 95%CI crossed the threshold of no effect.
f. The heterogeneity was estimated as moderate level ($Chi^2 = 1.82$, $P = 0.18$, $I^2 = 45\%$), but not significant.
g. The 95%CI excluded the threshold of null effect. However, the number of participants was smaller than 400, which was suggested by Grade Handbook for assuring the balance of prognosis.

Didgeridoo playing for sleep-related breathing problem

№ of participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							standard care	music playing		Risk with standard care	Risk difference with active music intervention
Sleep quality (assessed with: PSQI)											
25 (1 RCT)	serious [a]	not serious	not serious	serious [b]	none	⊕⊕◯◯ LOW	11	14	-	The mean sleep quality was 5.6	mean 1.3 lower (3.24 lower to 0.64 higher)

CI: Confidence interval

a. Random sequence generation was unclear. The blinding of patients was not done.
b. Sample size (N= 25) was small to ensure the prognostic balance.

Thesen

1. Musikhören kommt Erwachsenen mit Ein- und Durchschlafstörung zugute.
2. Bei Patienten mit Insomnie (unspezifisch) wirkt Musikhören signifikant, wenn es für mindestens 2 Wochen eingesetzt wird.
3. Bei Patienten mit spezifisch bedingter Insomnie ist die Wirkung des Musikhörens von der Behandlungsdauer abhängig.
4. Patienten mit Depression und chronischen Schmerzen benötigen eine längere Behandlungsdauer von Musikhören für mindestens 4 Wochen. Bei Tumorpatienten ist eine zweiwöchige Behandlung nötig.
5. Nach der Anwendung des Musikhörens für 1-3 Tage verbessert sich das Wohlbefinden der Patienten mit Schlafbeschwerden auf Intensivstation oder das der Patienten vor/nach einer Operation nachweislich. Dabei ist die Einschlafphase durch Musikhören verkürzt und die Tiefschlafphase verlängert.
6. Musikhören trägt zur Schlafentwicklung bei Frühgeborenen bei.
7. Musikhören (z.B. Mozart) reduziert bei Patienten die Anzahl schlafbezogener epileptischer Anfälle.
8. Didgeridoo-Spielen erleichtert schlafbezogene Atemprobleme.
9. Musik, die sich durch Ruhe, Langsamkeit, Entspannung, Instrumentalität, wenig dramatische Dynamik und sich wiederholende Muster auszeichnet, synchronisiert möglicherweise die Herzfrequenz mit der musikalischen Schlagfolge (60-80 bpm).
10. Die variierten Faktoren (z.B. Genre, Tonart, Rhythmus usw.) von Musik und deren komplizierten Kombinationen haben verschiedene Einflüsse auf Patienten mit Schlafstörungen.

Lebenslauf

Aichen C. Huang

PERSÖNLICHE ANGABEN
Familienstand: verheiratet, 2 Kinder
Geburtsdatum/-ort: 3. Februar 1985, Taiwan

Lutherstraße 70
06110 Halle(Saale)
Telefon: +49 (0) 176 41 50 90 25
Email: aichenh@googlemail.com

KURZPROFIL
Musiktherapie, klinische Musikforschung,
Verfahren der evidenzbasierten Medizin, Metaanalyse

AKADEMISCHER WERDEGANG

Seit 03/2012	**Doktorandin** an der Martin-Luther Universität Halle-Wittenberg Promotionsstudiengang Gesundheits- und Pflegewissenschaften: Partizipation als Ziel von Pflege und Therapie Dissertation: The effect of music on sleep disorders: a systematic review and meta-analysis (Die Wirkung der Musik auf Schlafstörungen: Eine systematische Übersichtsarbeit und Metaanalyse) 2014-05/2015 Elternzeit für zwei Kinder (0 Jahr / 1,5 Jahre)
10/2008-09/2010	**Musiktherapie (M.A.)** in der SRH Hochschule Heidelberg Masterthesis: Die Gestaltung der klinischen Improvisation: Diskurs der Technikebenen der klinischen Improvisation und deren Einsatz
2004-2007	Lehrgang zur Musiklehrerin am Zentrum für Lehrerbildung
2000-2007	Tainan Nationale Universität für Kunst. Hauptfach: Musik

AKADEMISCHE TÄTIGKEITEN

11/2017	4. PhD Kongress der Medizinischen Fakultät der Martin-Luther-Universität Halle-Wittenberg Posterpräsentation: Auswirkungen von Musik auf Menschen mit Schlafstörungen – Eine systematische Übersichtsarbeit und Meta-Analyse
12/2016	Konferenzbeitrag zur Schlafforschung und Schlafmedizin Posterpräsentation: *Auswirkungen von Musik auf Schlafstörungen – eine Meta-Analyse*
03/2013	Review Protokoll-Registrierung durch PROSPERO: *Aichen Huang, Gero Langer.*

The effects of music on sleep disorders. PROSPERO 2013:CRD42013004447
(http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42013004447)

PRAKTIKA/ ZERTIFIKAT

01/2010-09/2010	Co-Therapeutin und Monitoring in dem Forschungsprojekt der Hochschule Heidelberg (Musiktherapeutischer Schwerpunkt: chronische Schmerzen)
07/2009-09/2009	Musiktherapeutische Praktikantin in der Tagesklinik für Ältere und in der Palliativstation am städtischen Klinikum Karlsruhe
03/2009-06/2009	Trainerzertifikat für das „Entspannungstraining nach musiktherapeutischen Gesichtspunkten“
06/2007	Zertifikat für Musikerziehung

SOZIALES ENGAGEMENT

07/2010	Proof-Reading Projekt für die Wiedererlangungs-Übersetzung des neuen Testaments von Living Stream Ministry. (Die Aufgabe beinhaltete deutsch-englisch Comepare-reading)
2004-2010	Vielfältige Musikaufführungen: Freier Improvisation für vier Hände nach lateinischem Gefühl, Klavier Recital, Klavierkonzerts, Mandolinenkonzerte mit dem Mandolinenorchester, Klavierbegleitung in der Kirchengemeinde
2003-2007	Leiterin eines christlichen Studentenvereins an der Universität

Halle (Saale), am 1. Oktober 2017

(Unterschrift)

Selbständigkeitserklärung

Hiermit erkläre ich, dass die Angaben wahrheitsgemäß gemacht und die wissenschaftliche Arbeit an keiner anderen wissenschaftlichen Einrichtung zur Erlangung eines akademischen Grades eingereicht wurden. Die vorliegende Arbeit habe ich selbstständig und ohne fremde Hilfe verfasst habe. Alle Regeln der guten wissenschaftlichen Praxis wurden eingehalten. Zudem sind die Stellen, die von anderen Quellen entnommenen wurden, als solche kenntlich gemacht worden.

Ich versichere, dass niemand von mir unmittelbar oder mittelbar geldwerte Leistungen für Arbeiten erhalten, die mit dem Inhalt der vorgelegten Dissertation im Zusammenhang stehen. Bislang wurde die Arbeit weder im In- noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde vorgelegt.

Halle (Saale), am 1. Oktober 2017

(Unterschrift)

Erklärung über frühere Promotionsversuche

Ich erkläre, dass von mir bislang keine früheren Promotionsgesuche mit dieser Dissertation erfolgt sind. Es wurde nur dieser Antrag auf Eröffnung des Promotionsverfahrens eingereicht.

Halle (Saale), am 1. Oktober 2017

(Unterschrift)

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