Title
Recorded Music Listening Interventions for Symptom Management During Mechanical Ventilation in Critical Care

Author
Menza, Rebecca

Publication Date
2022

Peer reviewed|Thesis/dissertation

Recorded Music Listening Interventions for Symptom Management During Mechanical Ventilation in Critical Care

by

Rebecca Menza

DISSERTATION

Submitted in partial satisfaction of the requirements for degree of

DOCTOR OF PHILOSOPHY

in

Nursing

in the

GRADUATE DIVISION

of the

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Approved:

DocuSigned by:

Heather Leutwyler

012039073579437...

Heather Leutwyler

Chair

DocuSigned by:

Jill Howie-Esquivel

Jill Howie-Esquivel

DocuSigned by:

Julene Johnson

37F9228B23A9455...

Julene Johnson

Committee Members

Dedication and Acknowledgements

I dedicate this dissertation to all patients and families affected by trauma and critical care hospitalization, and in particular, those admitted to San Francisco General Hospital.

Developing these ideas, collecting this data and writing this dissertation has been consuming work for the past 5 years. No one does this sort of thing alone, there are many to thank and acknowledge. Dr Jill Howie-Esquivel, you have been my mentor for almost 20 years. It was your advice that guided me to the PhD program at UCSF; your clear direction that helped me achieve each milestone in this degree; your encouragement that gave me the confidence to do a mixed methods analysis and to perform primary data collection. Dr Heather Leutwyler, you are an unflappable source of encouragement. You've counseled me through this entire academic journey. Critically, you gave me the mentorship and courage to do a qualitative analysis, the results of which have changed my entire outlook on this topic and my future plans as a nurse scientist. Dr Julene Johnson, you've given me opportunities on the local and national scale and have pushed me to be more rigorous, helping me to grow as a budding scientist in the intersection of music and health. Dr Tom Hoffman, thank you for the mentorship, expertise, time, and endless encouragement.

Raising a PhD takes a village, or in my case a city. Dr Tasce Bongiovanni, I am so lucky to have your partnership as a clinician and a researcher; I'm constantly learning from you. You launched this ship for us and fueled it with optimism and pragmatism. Dr. Julin Tang, you were the person who introduced this concept to me, without you and your ongoing support, there would never have been a music study. Thank you to the Trauma Nurse Practitioner group who covered my shifts during deadlines, spread the word about music in the hospital, screened participants, talked through study design, and supported and encouraged me to collect data

through the pandemic and pursue this degree the first place. Rich Kallet, you helped me conceptualize an approach in the early days and gave me critical feedback and direction when it came to analysis and writing, thank you. And thank you to the staff respiratory therapists at SFGH who set up countless monitoring devices and (re)explained pulmonary mechanics to me every few months. To the UCSF surgery faculty, thank you for welcoming me as a scientist and for embracing the topics and outcomes I chose to explore.

To my PhD cohort, having a peer group and a shared experience made this possible, I've loved the warmth between us. To Ashely Younger, we were meant to be friends ($\kappa = 0.9$). You are so darn smart (and funny), I lucked out having you by my side these last 5 years.

To my husband Scott Compton, we've done a lot of hard things together. And while we have a loving and equal partnership, this hard thing, this degree was all about me. You made endless cups of tea, walked me up and down the hills of Berkeley, you encouraged me to keep going with primary data collection in a pandemic, waiting in cars to cheer me on. You were a coach, a manager, a physio and a teammate. To my family, who believed in me, and supported me to climb up on my father's shoulders, thank you. And to my dad, my first professor, I did this for both of us. You and me, the Dr's Menza.

Recorded Music Listening Interventions for Symptom Management During Mechanical Ventilation in Critical Care

Abstract

Rebecca Menza

Background: Over 4 million adults are admitted annually to intensive care units (ICU) in the US. Critically ill patients experience significant symptom burden including high rates of pain, anxiety, delirium, restlessness, dyspnea, confusion, sleep disorders, loneliness, depression, and fear. Advanced respiratory support with mechanical ventilation (MV) is the most common intervention used in critical care and is an independent risk factor for each of these co-occurring symptoms. Medications are of limited effectiveness for the management of many symptoms and also confer increased morbidity including worsening delirium, increased length of stay and the development of long-term psychological and cognitive problems. To mitigate these risks, guidelines for symptom management in the ICU include recommendations for the use of non-pharmacologic therapies such as music-based interventions.

Purpose: The purpose of this dissertation study is to analyze and synthesize existing literature that measures outcomes of recorded music listening interventions (RMLIs) for the management of common symptoms in critically ill adults during MV, and to describe the effects of listening to recorded music during critical care hospitalization.

Methods: This dissertation presents three manuscripts. The first is a systematic review summarizing the state of the evidence that examines RMLIs to manage common symptoms experienced by critically ill adults during MV using the 2009 PRISMA guidelines. The inclusion criteria were experimental and quasi-experimental designed studies published between January 1, 1998, and March 20, 2022. The quality of available evidence was evaluated using the

Evidence Project Risk of bias tool. The second study is a grounded theory analysis of patients' perceptions of the effects of listening to self-selected music on symptom experience during MV and critical care hospitalization. The third study examines the effects of a personally selected RMLI on ventilator-derived breathing measures of rate, depth and pattern during MV. Both prospective studies were conducted in the Surgical and Neurosurgical ICUs of a single, academic, urban, level-one trauma center and safety net hospital in San Francisco, California between August 2020, and November 2021.

Results: The results of the systematic review confirm that RMLIs are effective for the treatment of anxiety and pain and also identified other common symptoms such as agitation, that may be moderated by RMLIs in adults during MV. Most studies used investigator-selected music or restricted music to a limited selection of slow tempo recordings. The broad scope of the review and heterogeneity of outcome measures confounded synthesis of the results and precluded summative recommendations for RMLIs for symptom management but highlighted important literature gaps. Specifically, few studies measured the effect of RMLIs on common symptoms such as dyspnea, confusion, delirium, sleep, loneliness, and general distress. Physiologic signs did not vary with RMLI, underscoring the lack of reliable objective instruments that measure the effects of RMLI in patients unable to self-report. Results of the qualitative study show that listening to personally selected recorded music may be beneficial for cognitive and psychological recovery in ICU. Analysis of 14 semi-structured interviews, notes, and observations revealed 6 uses of personally selected music listening in ICU: 1) Restoring consciousness; 2) Maintaining cognition; 3) Humanizing the hospital experience; 4) Providing a source of connection; 5) Improving psychological wellbeing; and 6) Resolving the problems of silence. Recorded music was rarely used to address pain or anxiety. Instead, participants reported the use of recorded

music listening to address complex psychological experiences of loneliness, fear, de-situation, confusion, intrusive thoughts, threats to identity and loss of control through the use of music related memories and distraction. Listening to self-selected music provided a sense of self and a method to process trauma and grief. Additional benefits of listening to recorded music included feeling joy, pleasure, hope, resilience, and a sense of normalcy. Participants identified an aversion to being sedated as well as feelings of abandonment and restraint associated with silence. In the quantitative analysis, breathing measures theoretically associated with relaxation did not vary as hypothesized with an RMLI during both machine-controlled ventilation and spontaneous breathing modalities. In this pilot study of 16 critically ill adults during MV, analysis of breath-by-breath data did not demonstrate an effect of RMLIs on respiratory rate (breaths per minute), breath depth (tidal volume in liters or maximum pressure associated with fixed volume breaths), nor breath pattern (liters of breath per minute, breaths per liter per minute, inspiratory flow, and other indirect measures of work of breathing). The null results in this pilot were likely related to the magnitude of the variance within the small sample, high incidence of delirium, and the heterogeneity of the music selections in the intervention. Use of a noninvasive pulmonary mechanics monitor facilitated the collection of objective, rich, continuous data and is a feasible instrument that adds to the rigor of the findings.

Conclusions: The morbidity associated with the symptoms experienced during MV speak to the imperative to expand the access to and use of non-pharmacologic interventions for adults during critical care hospitalization. Listening to preferred, personally selected music represents a safe, widely acceptable, equitable intervention that is likely to be of benefit for the management of common psychological and cognitive symptoms not amenable to traditional medical interventions. Future studies that use validated instruments that address clinically meaningful

outcomes will provide scientific justification for the use of RMLIs and contribute to the understanding of the mechanism of action of RMLIs.

Table of Contents

List of Figures and Appendices

Chapter 1

Chapter 2

Chapter 3

Chapter 4

List of Tables

Chapter 2

Chapter 3

Chapter 4

List of Abbreviations

ANS, Autonomic Nervous System

BPS, Behavioral Pain Scale

CAM-ICU, Confusion Assessment Method for Intensive Care Units

COMET, Core Outcome Measures for Effectiveness Trials

CONSORT, Consolidated Standards of Reporting Trials

CPOT, Critical Care Pain Observation Tool

CVA, Cerebral Vascular Accident

DBP, Diastolic Blood Pressure

ETT, Endotracheal tube

FiO2, Fraction of Inspired Oxygen

HADS, Hospital Anxiety and Depression Scale

HR, Heart Rate

ICU, Intensive Care Unit

IPAT, Intensive Care Psychological Assessment Tool

L, Liters

MAP, Mean Arterial Blood Pressure OR Mean Airway Pressure

MBI, Music Based Intervention

MV, Mechanical Ventilation

NRS, Numbers Rating Scale

PADIS, Pain, Anxiety/Agitation, Delirium, Immobility and Sleep

PDI, Peritraumatic Distress Inventory

PEEP, Positive End Expiratory Pressure

PICS, Post Intensive Care Syndrome

PEF, Peak Expiratory Flow

PIF, Peak Inspiratory Flow

PIP, Peak Inspiratory Pressure

POMS, Profile of Mood States

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

PSV, Pressure Support Ventilation

PTSD, Post Traumatic Stress Disorder

RASS, Richmond Agitation Sedation Scale

RMLI, Recorded Music Listening Intervention

RR, Respiratory Rate

RSBI, Rapid Shallow Breathing Index

SBP, Systolic Blood Pressure

STAI, State-Trait Anxiety Inventory

TBI, Traumatic Brain Injury

U.S., United States

V_E, Minute Ventilation

V_T , Tidal Volume

VAS, Visual Analogue Scale

VCV, Volume Control Ventilation

Chapter 1: Introduction

Critically ill, mechanically ventilated (MV) adults experience high rates of distressing symptoms often treated with medications which may increase morbidity. Music-based interventions (MBIs) are guideline-recommended for symptom management and are the subject of increasing interest as clinicians seek non-pharmacological interventions for symptom management in this vulnerable population. Recorded music listening interventions (RMLIs) are an accessible form of MBIs for patients during MV. Data demonstrate the efficacy of RMLIs to improve self-reported pain and anxiety in MV adults but evidence to support the use of RMLIs for other important symptoms and evidence of efficacy in populations unable to self-report is still lacking. This research aims to identify symptoms that may benefit from RMLIs in critically ill patients and potential measures of the effects of RMLIs to support an evidence-based expansion of their use for MV adults. This chapter will: 1) Introduce the dissertation study by first discussing the background and context of the problem of symptom management in critical care, 2) Define RMLIs and describe the evidence for their use in symptom management, and 3) Explicate the theoretical framework used to support the study, and 4) State the overall purpose of the study and the specific aims.

Symptom Experience of Mechanically Ventilated, Critically Ill Adults

More than 4 million adults are admitted annually to intensive care units (ICU) in the US (1). Advanced respiratory support with mechanical ventilation (MV) is the most common intervention used in critical care (1). Between 20-40% of adults receive MV during their ICU admission and The Global Burden of Disease Project estimates that worldwide, MV is used for 13-20 million people annually (1, 2). MV adults experience longer lengths of stay (14.4 days,

compared to 8.5) and incur an increased cost of care compared to non-MV adults ($31,574 vs $12, 931) (3).

Pain, anxiety, dyspnea and sleep disruption are among the most common symptoms reported by critically ill adults (4-7). In addition, patients in ICU experience cognitive and psychological symptoms such as confusion, fear, loneliness, and sadness (6, 7). Distressing symptoms are more prevalent and more intense during MV (4, 5, 7, 8). Over 50% of MV adults report pain during procedures such as suctioning and turning and 33% experience pain while at rest (9). Rates of anxiety increase from 50% in the general ICU population to 80% during MV (7, 10, 11). Distressing symptoms are often co-occurring, and many potentiate one another. For example, anxiety and depression increase acute pain (12) and fear contributes to dyspnea during MV. Agitation is used to describe a hyperactive, distressed state in patients unable to communicate and may be caused by pain, anxiety, confusion, or dyspnea (13). MV is also an independent risk factor for the development of delirium occurring in up to 70% of MV adults (14, 15). Delirium causes physical and emotional distress and may affect recovery resulting in increased length of MV, longer ICU stays and long-term cognitive impairment and death (16-21). Additionally, undermanaged symptoms such as distress, anxiety, confusion and fear delay the success of MV weaning trials, prolonging the length of MV and leading to increased length of stay.

Failure to adequately address distressing symptoms during ICU hospitalization can have both immediate and long-term consequences. In addition to the symptoms experienced by MV patients during ICU hospitalization, many ICU survivors experience a constellation of persistent symptoms called post-intensive care unit syndrome (PICS) consisting of anxiety, depression, post-traumatic stress, cognitive impairment, functional disability, and decreased quality of life

(22, 23). According to the Society of Critical Care Medicine, between 30-80% of adults have some degree of new cognitive deficit at the time of discharge from the ICU; many are burdened with intrusive thoughts and most have difficulty with sleep (1). Additionally, 64% of adult ICU survivors experience at least one symptom of PICS 3 months after ICU hospitalization and over half are still affected at 12 months (24). Quality and type of ICU memories are predictors of post-traumatic stress disorder and PICS in ICU survivors (25). Modifiable risk factors for PICS include negative ICU experiences and development of delirium during hospitalization (26).

Safe symptom management in critical care remains a challenge. Opioids, a mainstay for treatment of acute pain in critical care, may worsen delirium; conversely, under-treated pain may precipitate delirium (27). Benzodiazepines, antipsychotics, and hypnotic sedatives used to manage confusion, agitation and delirium are of limited effectiveness and are associated with increased morbidity including worsening delirium, prolonged MV and longer length of stay (20, 28, 29). Many troubling ICU memories are shaped by hallucinations, a feature of delirium, and are associated with benzodiazepine use (30). However, lower sedation level has also been associated with increased perception of and negative memories of ICU hospitalization, which may increase the risk of posttraumatic stress disorder and PICS (31). Current practice recommendations are to minimize psychoactive medications and to employ therapies that address upstream causes of agitation such as fear, sleep disturbance, communication deficits, dyspnea, and pain (18). New guidelines for the management of pain, anxiety, agitation, and delirium in the ICU also include recommendations for the use of non-pharmacologic therapies, such as MBIs (32).

Recorded Music Listening Interventions

Music has a near universal appeal. Listening to music stimulates a variety of emotions, feelings and neurobiological effects (33). Listening to music may have effects on the limbic and hypothalamic-pituitary axis resulting in physical signs and psychological reports of relaxation, anxiolysis, and emotional reward (34-36). Specifically, psychobiological responses are thought to be activated by an emotional response to music, based on memories of music and cognitive processing of musical stimuli (37, 38).

The use of music for therapeutic benefit has been practiced for centuries by a wide range of people. Empiric studies examining the use of music to treat conditions of mania, depression, and anxiety date to the mid-18th century (39). The therapeutic use of music by nurses can be traced to Florence Nightingale who advocated for the use of music for symptom management in her sentinel *Notes on Nursing* (40).

When music is used in the clinical setting to achieve a health-related goal, it is called a music-based intervention (MBI) (41). MBIs are defined by Robb et al as 'the use of music to manage symptoms, improve quality of life, promote physical and/or psychosocial function and/or promote well-being'(42). Therapeutic MBIs are classified as either 'active', such as making music, playing an instrument, or singing, or as 'receptive', such as listening to music (43). MBIs may be delivered by a credentialled music therapist (music therapy) or by a health care provider (music medicine) (43, 44). Recorded music listening interventions (RMLIs) are one type of MBI and may be administered by nurses without specialized training.

MBIs (all sorts) feature in several nursing practice guidelines for the non-pharmacologic treatment of distressing symptoms (41, 45). Data show that critical care nurses support the use of MBIs for symptom management in critical care and that listening to recorded music is among the

most frequent patient- requested non-pharmacologic therapies (46-48). Recommendations for music selections targeting dyspnea, pain, anxiety and sleep disturbances in critical care are that the recorded music be familiar, tailored to patient preference, be of a 'relaxing' nature, and at least 20-30 minutes in length (41, 45). Music preference varies widely and is influenced by social, cultural, and personal factors (35). Prior research includes the use of a music assessment tool (49) to develop a patient preferred playlist; however, tools such as these are limited to genres or specific albums and do not make available the variety of music choice or artificial intelligence music selection features now widely accessible through advances in technology including app-based programs or services.

Recorded Music Listening Interventions for Symptom Management in Critical Care

Advances in cognitive neuroscience and the imperative to deliver evidence-based practice have led to a rise in the quantity and quality of research examining the health benefits of listening to music in health care settings. MBIs are the most commonly studied complementary health interventions for symptom management in critical care (50). A recent systematic review of MBIs use in critically ill adults showed that MBIs of 20-30 minutes in length are efficacious for the reduction of self-reported pain, but the same review was unable to determine a benefit for people unable to self-report (51). Self-reported anxiety scores have also been reduced with MBIs in MV adults (52). However, the effect of MBIs on objective measures of pain and or other important symptoms such as sleep, agitation, confusion and delirium, and dyspnea has not been established. Furthermore, the specific use of RMLIs for symptom management has not been evaluated as prior systematic reviews do not distinguish between type of MBI and include live music therapy interventions alongside nurse administered RMLIs.

Theoretical Framework: Nightingale's Theory of Nursing (and the Environment) and Damasio's Theory of Emotion, Feeling and Core Consciousness

This dissertation is informed by two theories, Florence Nightingale's Theory of Nursing (and the Environment) and Antonio Damasio's Theory of Emotion, Feeling and Core Consciousness (Figure 1.1). Both theories are grounded in principles of Holism, a philosophy that emphasizes the connection between the body and the mind and acknowledges the bidirectional and aggregate relationship between the two (53). Damasio postulates that feelings in the body (somatic markers), emotions (in the brain) and consciousness (in the mind) work together to achieve homeostasis, and that physical and emotional survival are dependent on these relationships (37). According to Damasio, music, a strong auditory stimulus, is processed in several parts of the brain including areas responsible for emotional and physical regulation. Nightingale's Theory of Nursing (and the Environment) is also predicated on connections between mind, body, and environment (40). Nightingale insisted that knowledge of a whole *person* is greater than that which can be derived from any one symptom or sign. According to the principles of Holism, the effective management of distressing symptoms in MV adults requires comprehensive assessment and treatment of co-occurring symptoms and may be successfully accomplished through the use of potent cognitive stimuli such as music.

Purpose and Specific Aims

The overall purpose of this dissertation study is to analyze and synthesize existing literature that measures outcomes of recorded music listening interventions (RMLIs) for the management of common symptoms in critically ill adults during MV, and to describe the effects of listening to recorded music during critical care hospitalization.

The specific aims of this study are:

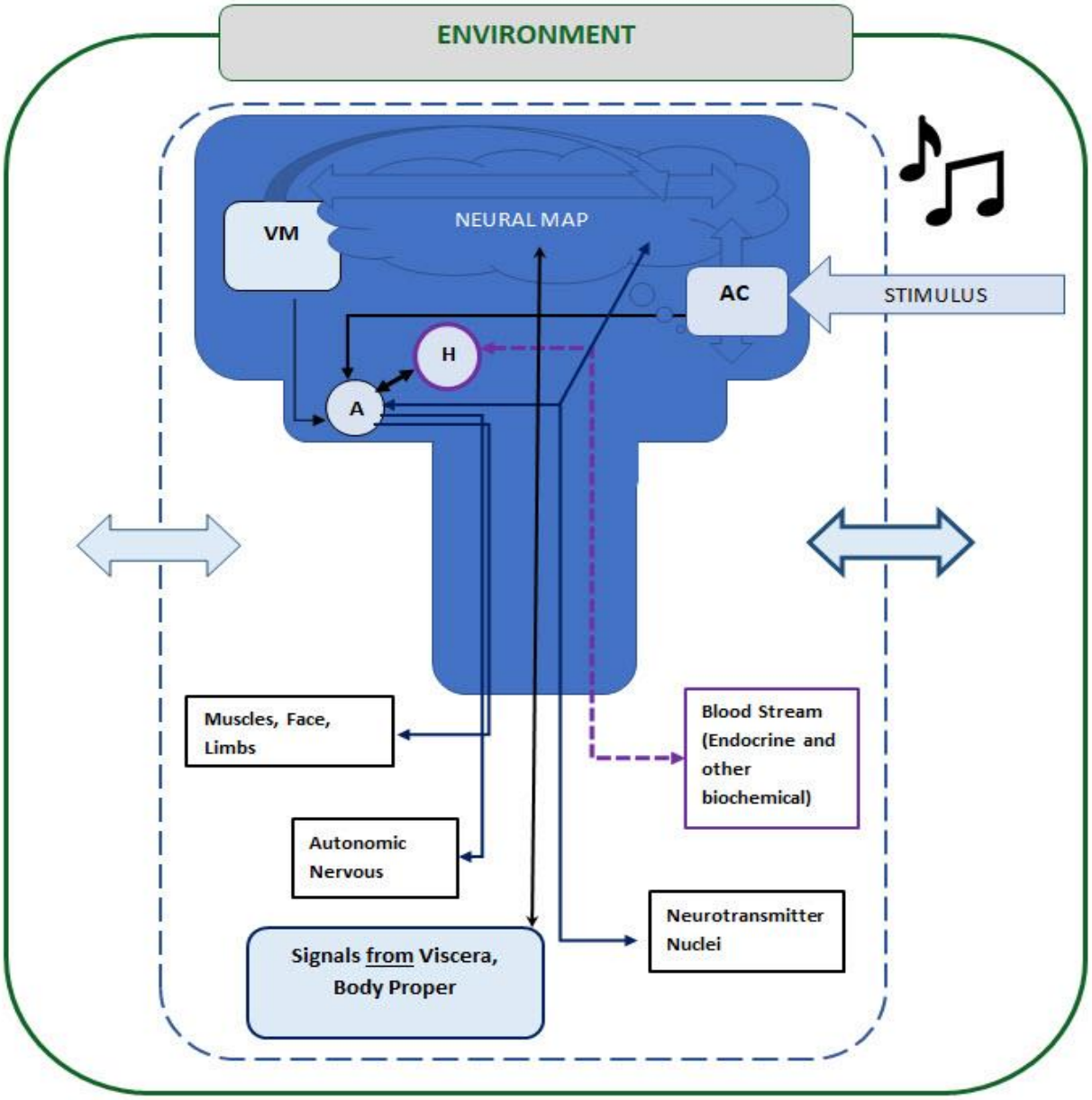
AIM 1: Evaluate the state of the evidence that measures the effect of RMLIs on symptoms of pain, anxiety, agitation, sedation, delirium, sleep disorders, distress, loneliness, or fear, during MV in critical care.

AIM 2: Describe patients' perceptions of the effects of listening to self-selected music on symptom experience during MV after critical injury.

AIM 3: Evaluate the effects of an RMLI on breathing measurements of rate, depth, and pattern in critically injured adults during MV.

Presentation of the Dissertation

This dissertation is presented in 5 chapters. Chapter 1 introduces the background and significance of the study as well as the purpose and specific aims of the dissertation. Chapter 2 is a systematic review of the literature of existing research that measures the effect of RMLIs on common symptoms experienced during MV. Chapter 3 is a qualitative study that explores the perceived benefit and use of listening to personally selected, recorded music among a diverse group of adults experiencing critical care hospitalization. Chapter 4 is an exploratory data-based pilot study that examines the effect of an RMLI on measures of breathing derived from ventilators during MV in a sample of adults. Chapter 5 provides a summary of findings, discusses strengths and limitations of the study, and offers recommendations for future research and nursing implications.



Key: A: Amygdala; AC: Auditory Cortex; H: Hypothalamus; VM: Ventromedial Cortex

Figure 1.1: **Proposed psychoneurobiological response to music, an application of Damasio's Theory of Emotion, Feeling and Consciousness with Florence Nightingale's Theory of the Nursing and the Environment, adapted from Hannah Damasio, Damasio, 1994.**

References

1. SCCM. http://www.sccm.org/Communications/Pages/CriticalCareStats.aspx 2018
2. Adhikari NK, Fowler RA, Bhagwanjee S, Rubenfeld GD. Critical care and the global burden of critical illness in adults. Lancet (London, England). 2010;376(9749):1339-46.
3. Dasta JF, McLaughlin TP, Mody SH, Piech CT. Daily cost of an intensive care unit day: the contribution of mechanical ventilation. Critical care medicine. 2005;33(6):1266-71.
4. Granberg A, Bergbom Engberg I, Lundberg D. Patients' experience of being critically ill or severely injured and cared for in an intensive care unit in relation to the ICU syndrome. Part I. Intensive & critical care nursing. 1998;14(6):294-307.
5. Rotondi AJ, Chelluri L, Sirio C, Mendelsohn A, Schulz R, Belle S, et al. Patients' recollections of stressful experiences while receiving prolonged mechanical ventilation in an intensive care unit. Critical care medicine. 2002;30(4):746-52.
6. Topcu S, Alpar S, Karabacak B, Kebapcı A. Patient experiences in intensive care units: a systematic review. Patient Experience Journal. 2017;4:115-27.
7. Puntillo K, Arai S, Cohen N, Gropper M, Neuhaus J, Paul S, et al. Symptoms experienced by intensive care unit patients at high risk of dying. Critical care medicine. 2010;38(11):2155-60.
8. Thomas LA. Clinical management of stressors perceived by patients on mechanical ventilation. AACN Clin Issues. 2003;14(1):73-81.
9. Payen JF, Chanques G, Mantz J, Hercule C, Auriant I, Leguillou JL, et al. Current practices in sedation and analgesia for mechanically ventilated critically ill patients: a prospective multicenter patient-based study. Anesthesiology. 2007;106(4):687-95; quiz 891-2.

10. Li DT, Puntillo K. A pilot study on coexisting symptoms in intensive care patients. Applied nursing research : ANR. 2006;19(4):216-9.
11. Puntillo K, Nelson JE, Weissman D, Curtis R, Weiss S, Frontera J, et al. Palliative care in the ICU: relief of pain, dyspnea, and thirst--a report from the IPAL-ICU Advisory Board. Intensive care medicine. 2014;40(2):235-48.
12. Michaelides A, Zis P. Depression, anxiety and acute pain: links and management challenges. Postgraduate medicine. 2019;131(7):438-44.
13. Tate JA. Anxiety and Agitation in Mechanically Ventilated Patients. 2012;22(2):157-73.
14. Von Rueden KT, Wallizer B, Thurman P, McQuillan K, Andrews T, Merenda J, et al. Delirium in Trauma Patients: Prevalence and Predictors. Crit Care Nurse. 2017;37(1):40-8.
15. Zaal IJ, Devlin JW, Peelen LM, Slooter AJ. A systematic review of risk factors for delirium in the ICU. Critical care medicine. 2015;43(1):40-7.
16. Lat I, McMillian W, Taylor S, Janzen JM, Papadopoulos S, Korth L, et al. The impact of delirium on clinical outcomes in mechanically ventilated surgical and trauma patients. Critical care medicine. 2009;37(6):1898-905.
17. Pandharipande P, Cotton BA, Shintani A, Thompson J, Pun BT, Morris JA, Jr., et al. Prevalence and risk factors for development of delirium in surgical and trauma intensive care unit patients. The Journal of trauma. 2008;65(1):34-41.
18. Barr J, Fraser GL, Puntillo K, Ely EW, Gelinas C, Dasta JF, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Critical care medicine. 2013;41(1):263-306.

19. Burry LD, Williamson DR, Mehta S, Perreault MM, Mantas I, Mallick R, et al. Delirium and exposure to psychoactive medications in critically ill adults: A multi-centre observational study. Journal of critical care. 2017;42:268-74.

20. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. Anesthesiology. 2006;104(1):21-6.

21. Ouimet S, Kavanagh BP, Gottfried SB, Skrobik Y. Incidence, risk factors and consequences of ICU delirium. Intensive care medicine. 2007;33(1):66-73.

22. Nikayin S, Rabiee A, Hashem MD, Huang M, Bienvenu OJ, Turnbull AE, et al. Anxiety Symptoms in Survivors of Critical Illness: A Systematic Review and Meta-Analysis. General hospital psychiatry. 2016;43:23-9.

23. Lof L, Berggren L, Ahlstrom G. ICU patients' recall of emotional reactions in the trajectory from falling critically ill to hospital discharge: follow-ups after 3 and 12 months. Intensive & critical care nursing. 2008;24(2):108-21.

24. Marra A, Pandharipande PP, Girard TD, Patel MB, Hughes CG, Jackson JC, et al. Co-Occurrence of Post-Intensive Care Syndrome Problems Among 406 Survivors of Critical Illness. Critical care medicine. 2018;46(9):1393-401.

25. Svenningsen H, Egerod I, Christensen D, Tonnesen EK, Frydenberg M, Videbech P. Symptoms of Posttraumatic Stress after Intensive Care Delirium. BioMed research international. 2015;2015:876947.

26. Lee M, Kang J, Jeong YJ. Risk factors for post-intensive care syndrome: A systematic review and meta-analysis. Aust Crit Care. 2020;33(3):287-94.

27. Daoust R, Paquet J, Boucher V, Pelletier M, Gouin É, Émond M. Relationship Between Pain, Opioid Treatment, and Delirium in Older Emergency Department Patients. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2020;27(8):708-16.

28. McGrane S, Pandharipande PP. Sedation in the intensive care unit. Minerva anestesiologica. 2012;78(3):369-80.

29. Girard TD, Kress JP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomized controlled trial. Lancet (London, England). 2008;371(9607):126-34.

30. Parker AM, Sricharoenchai T, Raparla S, Schneck KW, Bienvenu OJ, Needham DM. Posttraumatic stress disorder in critical illness survivors: a metanalysis. Critical care medicine. 2015;43(5):1121-9.

31. Samuelson KA, Lundberg D, Fridlund B. Stressful experiences in relation to depth of sedation in mechanically ventilated patients. Nursing in critical care. 2007;12(2):93-104.

32. Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJC, Pandharipande PP, et al. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Critical care medicine. 2018;46(9):e825-e73.

33. Habibi A, Damasio A. Music, feelings, and the human brain. US: Educational Publishing Foundation; 2014. p. 92-102.

34. Zatorre RJ. Musical pleasure and reward: mechanisms and dysfunction. Annals of the New York Academy of Sciences. 2015;1337:202-11.

35. Farnsworth P. The Social Psychology of Music. 2nd ed. Ames, Iowa: The Iowa State University Press 1969. 298 p.

36. Fancourt D, Ockelford A, Belai A. The psychoneuroimmunological effects of music: a systematic review and a new model. Brain, behavior, and immunity. 2014;36:15-26.

37. Damasio A. Descartes' Error. Emotion, Reason, and the Human Brain. New York: Grosset Putnam; 1994.

38. van den Bosch I, Salimpoor VN, Zatorre RJ. Familiarity mediates the relationship between emotional arousal and pleasure during music listening. Frontiers in Human Neuroscience. 2013;7:534.

39. Gouk P. An Enlightenment proposal for music therapy: Richard Brocklesby on music, spirit, and the passions. Progress in brain research. 2015;217:159-85.

40. Nightingale F. Notes on Nursing. What It Is, And What It Is Not. Edinborough: Churchil Livingstone; 1859/1980.

41. Tracy MF, Chlan L. Nonpharmacological Interventions to Manage Common Symptoms in Patients Receiving Mechanical Ventilation. Critical Care Nurse. 2011;31(3):19-29.

42. Robb SL, Hanson-Abromeit D, May L, Hernandez-Ruiz E, Allison M, Beloat A, et al. Reporting quality of music intervention research in healthcare: A systematic review. Complementary therapies in medicine. 2018;38:24-41.

43. Sihvonen AJ, Särkämö T, Leo V, Tervaniemi M, Altenmüller E, Soinila S. Music-based interventions in neurological rehabilitation. The Lancet Neurology. 2017;16(8):648-60.

44. Stegemann T, Geretsegger M, Phan Quoc E, Riedl H, Smetana M. Music Therapy and Other Music-Based Interventions in Pediatric Health Care: An Overview. Medicines (Basel, Switzerland). 2019;6(1):25.

45. Fontaine DK. Nonpharmacologic management of patient distress during mechanical ventilation. Critical care clinics. 1994;10(4):695-708.

46. Tracy MF, Lindquist R, Savik K, Watanuki S, Sendelbach S, Kreitzer MJ, et al. Use of complementary and alternative therapies: a national survey of critical care nurses. Am J Crit Care. 2005;14(5):404-14; quiz 15-16.

47. Cooke M, Mitchell M, Tiralongo E, Murfield J. Complementary and alternative medicine and critical care nurses: a survey of knowledge and practices in Australia. Aust Crit Care. 2012;25(4):213-23.

48. Cutshall S, Derscheid D, Miers AG, Ruegg S, Schroeder BJ, Tucker S, et al. Knowledge, attitudes, and use of complementary and alternative therapies among clinical nurse specialists in an academic medical center. Clin Nurse Spec. 2010;24(3):125-31.

49. Chlan L, Heiderscheit A. A Tool for Music Preference Assessment in Critically Ill Patients Receiving Mechanical Ventilatory Support. Music therapy perspectives. 2009;27(1):42-7.

50. Thrane SE, Hsieh K, Donahue P, Tan A, Exline MC, Balas MC. Could complementary health approaches improve the symptom experience and outcomes of critically ill adults? A systematic review of randomized controlled trials. Complementary therapies in medicine. 2019;47:102166.

51. Richard-Lalonde M, Gélinas C, Boitor M, Gosselin E, Feeley N, Cossette S, et al. The Effect of Music on Pain in the Adult Intensive Care Unit: A Systematic Review of Randomized Controlled Trials. Journal of Pain and Symptom Management. 2020;59(6):1304-19.e6.

52. Bradt J, Dileo C. Music interventions for mechanically ventilated patients. The Cochrane database of systematic reviews. 2014;2014(12):Cd006902.

53. Light KM. Florence Nightingale and holistic philosophy. J Holist Nurs. 1997;15(1):25-40.

Chapter 2: Recorded Music Listening Interventions for Symptom Management in Critically Ill, Mechanically Ventilated Adults: A Systematic Review of the Literature

Abstract

Background: Mechanically ventilated (MV) patients in intensive care units (ICU) experience pain, anxiety, dyspnea, sleep disturbances, fear, and confusion. Medications used to treat these symptoms are associated with increased rates of delirium and longer length of stay. To mitigate these risks the Society of Critical Care Medicine recommends the judicious use of medication and the use of non-pharmacologic therapies such as music-based interventions. Listening to music has been associated with reductions in self-reports of anxiety in MV adults, however its use as an adjunct for the management of other distressing symptoms has not been evaluated.

Methods: A systematic search of the literature was conducted for studies that measured the efficacy of a recorded music listening intervention (RMLI) for symptom management in critically ill, MV adults between January 1, 1998, and March 20, 2022. Experimental designed trials that included a recorded music intervention tested against a comparator condition were included. The outcome measure of symptom management was assessed as an observed sign or a self-report of change in symptom experience.

Results: Electronic databases PubMED, EMBASE, CINAHL and Web of Science were searched. Of the 673 abstracts reviewed, 28 clinical trials were included in this review. The overall risk of bias was moderate. RMLIs were mostly delivered with headphones and used investigator-selected music, or patient-chosen music from a limited selection. RMLIs were associated with reduced pain and agitation, improved tolerance of MV and increased sedation levels when measured with validated psychometric tools. Patients able to communicate reported decreased pain, anxiety,

dyspnea, and distress. Delirium incidence and severity were unaffected by music listening. No studies measured sleep, fear, or loneliness. Vital signs were not changed by RMLIs.

Conclusions: Data demonstrate improved self-reported symptom experience and reductions in observed measures of agitation and pain after a RMLI in critically ill, adult MV patients. RMLIs are a low risk, non-pharmacological therapy that may improve distressing symptoms experienced by MV adults. More studies are needed to identify clinically meaningful outcomes and reliable measurements of the effects of RMLIs in MV patients unable to self-report.

Keywords: Music, Music Therapy, Music Based Intervention, Mechanical Ventilation, Critical Care, Sedation, Agitation, Anxiety, Pain, Delirium, Symptoms, Dyspnea, Distress, Sleep, Systematic Review

Introduction

Over 4 million adults are admitted annually to intensive care units (ICU) in the US where between 20-40% will receive advanced respiratory support with mechanical ventilation (MV) (1). Global estimates of MV use are between 13-20 million people per year (2). Critically ill patients experience significant symptom burden including high rates of pain, anxiety, delirium, restlessness, dyspnea, confusion, sleep disorders, loneliness, depression, and fear (3-6). MV is an independent risk factor for each of these co-occurring symptoms (7, 8). For example, rates of anxiety increase from 50% in the general ICU population to 80% in MV patients (9-11), and fear contributes to dyspnea in MV adults (12). Agitation, an observed constellation of physiologic, behavioral, and psychological responses may be caused by fear, sleep disturbance, communication deficits, anxiety, breathlessness, and pain (13, 14). People who experience delirium may be agitated or somnolent, some endorse hallucination, and others experience confusion (15). Delirium is also associated with poor outcomes such as increased length of MV, longer ICU stays, and long-term cognitive impairment (13, 16-20). Prior research suggests that people receiving MV also experience disembodiment exacerbated by lack of power and control over their environment and inability to communicate (21). In addition to the distress experienced by MV patients *during* ICU hospitalization, symptoms of pain, anxiety, delirium, and lack of sleep are associated with *post*-ICU anxiety, post-traumatic stress disorder (PTSD), depression and decreased quality of life at 1 year follow up (22, 23). Thus, failure to adequately address symptoms during ICU hospitalization can have long term health consequences.

Palliation of ICU symptoms remains a challenge. Common pharmacologic treatments for pain, anxiety, and agitation such as opioids, benzodiazepines, psychoactive medications, and continuous hypnotic infusions confer increased risk of delirium. Deeper levels of sedation used to

subdue severely agitated patients or to promote tolerance of MV are also associated with development of delirium and increased length of stay (24, 25). Consequently, total sedative burden reduction in ICU is strongly recommended (26). However, lighter sedation has also been associated with increased negative memories of ICU hospitalization, which increase the risk of PTSD (27). In an effort to strike a balance between excessive and inadequate medication, new guidelines for critically ill adults include recommendations to minimize psychoactive medications and to employ non-pharmacologic interventions, such as music, to reduce distressing symptoms associated with critical illness and MV(28).

Recorded Music Listening Interventions for Symptom Management in Critical Care

Empiric studies examining the use of music date back to the mid-18th century (29) and Nightingale advocated that music be used for symptom management (30). Symptom assessment and management is a hallmark of the nursing profession as explained in the UCSF Symptom Management Theory (31). According to Robb, music-based interventions (MBIs) are 'the use of music to manage symptoms, improve quality of life, promote physical and/or psychosocial function and/or promote well-being' (32). The use of MBIs to manage pain and anxiety appear in summary recommendations as easy to use, low risk interventions to promote safe and effective analgesia, anxiolysis, and sleep hygiene in critical care (11, 13, 33, 34). Whereas music therapy is delivered by a trained and licensed music therapist, other MBIs such as listening to recorded music may be initiated by nurses or other clinicians without specialized training (35). Nurses report interest and belief in the efficacy of recorded music listening interventions (RMLI) for symptom management in critical care, identifying music as one of the most requested modalities among their patients (36-38). As such, the use of RMLI represents an accessible and acceptable form of non-pharmacological intervention for symptom management in hospital settings.

The use of MBIs for symptom management in critical care has been reviewed before with mixed results. In one systematic review, the use of MBIs in critically ill adults was associated with reductions in self-reported pain, but not in observed pain scores (39). Others have reviewed the use of MBIs for the treatment of anxiety and stress in critically ill adults, noting similar reductions in self-reported symptom experience, but no change in objective measures (40). Garcia Guerra and colleagues also did not find evidence that MBIs were associated with reductions in sedative or analgesic use in their systematic review of MBIs in critical care (41). Bradt and Dileo examined the use of MBIs in MV adults and found reductions in self-reported anxiety scores, though the overall quality of evidence in their meta-analysis was low or very low (42). Study participants were restricted to awake, calm patients who could report their anxiety thereby limiting the generalizability of their results. Prior reviews also include a variety of MBIs, combining music therapy, live music and RMLI delivered by clinicians. As a result, the efficacy of a RMLI for symptom management remains unclear.

The imperative to treat distressing symptoms in MV patients while avoiding medication side effects has led to a rise in the number and the quality of randomized controlled trials (RCTs) available to inform practice. Despite evidence that distressing symptoms are co-occurring most studies of RMLI in MV adults are limited to the examination of a single symptom such as self-reported anxiety or pain, ignoring the relationship of co-occurring symptoms of dyspnea, depression, fear, delirium, and confusion. Studies of RMLIs in MV adults often exclude patients with altered mental status. If RMLIs can help reduce distress and medication burden , it is necessary to measure the effects against clinical outcomes of symptom relief in a population unable to self-report. Therefore, the purpose of this systematic review is to evaluate the state of

the evidence that utilizes a RMLI to manage common symptoms experienced by critically ill MV adults.

Methods

Protocol and Eligibility Criteria

This systematic review was conducted in accordance with the 2009 PRISMA guidelines (43, 44) and the protocol was registered on PROSPERO (CRD42020153026).

We included peer reviewed, experimental RCTs or quasi experimental trials published since 1998 that evaluated the effect of a recorded music listening intervention on commonly reported symptoms of pain, anxiety, agitation, delirium, confusion, dyspnea, sleep disturbances, fear, depression, and loneliness in critically ill MV adults (Table 2.1). For the purposes of this review, a RMLI was defined as a prescribed period of listening to pre-recorded music. Clinical trials that compared the use of music to "no music" or other comparator were included. This review was limited to clinical trials that assessed recorded music specifically; studies in which music was co-administered as part of a larger protocol of other interventions were excluded as were studies that included live music or non-music auditory stimulus (e.g., nature sounds). Language was restricted to studies written in English or French due to evaluator language ability. Further, studies were excluded if they had a qualitative design, or were review articles, published protocols, or cost effectiveness trials. Commentaries and editorials were also excluded. Participants were limited to adults, aged 18 and older, admitted to critical care areas including medical or surgical ICUs, and who were receiving MV. Studies including neonates, children, or mothers of neonates in critical care were excluded as were studies conducted exclusively in the operating room, procedural suite, or recovery room. Patients who were treated for burns were also excluded as this patient population experiences uniquely high levels of stress, anxiety and pain

which may influence the outcome of a RMLI and the reliability of findings across studies. Studies that examined primary outcome measures of objective assessment of sedation, agitation, relaxation, behavioral pain, ventilator tolerance, or sedative/analgesic medication burden were included as well as studies that measured subjective reports of dyspnea, pain, anxiety, sleep disturbances, confusion, loneliness, fear, and satisfaction. Articles whose outcomes were not measures of symptom burden were excluded.

Information Sources and Search Strategy

An initial exploratory search was conducted in consultation with a university librarian. Once the search terms were refined, studies were identified using search strategies within PubMed, Embase, CINAHL and Web of Science databases. Dates were restricted to 1/1/1998 – 3/20/2022 for all 4 searches. Medical Subject Heading (MeSH) search terms and free text words were systematically combined to identify relevant studies. The search strategy was adapted to each database after adding Boolean operators such as "AND/OR". Search terms are presented in Appendix 1. A grey literature search was conducted (RM) using reference lists from identified studies of interest.

Study Selection

Relevant results were scanned for duplicates. Next, the eligible studies were exported into Covidence software where the title and abstracts were screened by 2 independent reviewers (RM, TB) using the eligibility criteria. Studies that did not meet inclusion criteria were removed. The remaining articles that met inclusion criteria were screened by full text assessment. Studies that did not specifically measure distressing symptoms or related outcomes of an RMLI in MV adults in critical care settings were removed. A third reviewer (JHE) adjudicated any disagreements.

Data Collection and Items

Data were extracted from included studies through full text review by one investigator (RM). Extracted study variables included: author; setting; study design; sample size; demographic variables; and clinical characteristics at enrollment. Characteristics of RMLIs were identified according to CONSORT guidelines for reporting music-based interventions and extracted into a table (45). Extracted outcomes included: physiological measurements of heart rate (HR), respiratory rate (RR), systolic and diastolic blood pressure (SBP and DBP), oxygen saturation, Bispectral index of sedation (BIS), and change in electroencephalogram (EEG); observed measures of pain, delirium sedation or agitation; and subjective reports of anxiety, pain, dyspnea and distress using visual analogue scales (VAS), the State Trait Anxiety Index (STAI), Numeric Rating Scale (NRS) and the patient distress index (PDI). Due to the heterogeneity of symptoms and outcomes measured, a meta-analysis of findings could not be performed. A narrative synthesis of the findings was conducted and presented in text and tables. Any qualitative observations were extracted into Appendix 2.1.

Risk of Bias

Risk of bias was determined by 2 reviewers (RM, TB) using the Evidence Project risk of bias tool (46). The tool consists of 8 criteria designed to assess risk of bias across a variety of study designs including quasi experimental and observational studies and has a high inter-rater reliability (κ=0.66). Each manuscript was assessed for its adherence to the criteria including: (1) cohort, (2) control or comparison group, (3) pre-post intervention data, (4) random assignment of participants to the intervention, (5) random selection of participants for assessment, (6) follow-up rate of 80% or more, (7) comparison group equivalence on socio-demographics, and (8) comparison group equivalence at baseline on outcome measures. Because clinical

characteristics may influence the results of RMLIs in critical care, the category of 'baseline' demographics was expanded to include important clinical characteristics such as length of stay, length of mechanical ventilation, and diagnoses.

Results

Study Selection

The literature search revealed a total of 900 citations for review. After removing duplicates, 633 studies remained. After review of title and abstract, 573 did not meet screening criteria and were eliminated. The full text of the remaining 60 manuscripts were then assessed. Of these, 32 more were excluded because they did not meet inclusion criteria. A total of 28 studies were identified for final analysis (Figure 2.1). Two citations (47, 48) were identified from the same research study and are reported together.

Risk of Bias

None of the studies included in this review met all 8 criteria of rigor outlined in the Evidence Project risk of bias tool, resulting in an overall medium risk of bias (Table 2.2). Criteria that address 'participant representativeness' were the most commonly missing, specifically: 'random selection of participants' and 'follow up rates of at least 80%'. Random selection of participants is difficult in single center or critical care studies with strict inclusion criteria. High rates of attrition are common in critical care studies where sudden changes in clinical condition (including unanticipated improvements) interrupt studies conducted over days. Notably, studies that examined a single music listening intervention had high completion rates. Overall, study participants were well matched across treatment arms for socio-demographic measures. Critically, comparison groups were also equivalent across important, potentially confounding clinical features. While not formally assessed in the Evidence Project risk of bias tool, we embedded this

observation into the analysis of 'socio-demographic' equivalence between groups, potentially increasing the rigor of the tool.

Parity of baseline outcome measures between comparison groups was largely balanced adding to the validity of findings. Sample size, effect size and power analysis do not feature in the Evidence Project risk of bias tool and would likely add significant risk of bias to several of the studies included. Many were exploratory, pilot, or feasibility studies with small sample sizes and were not designed to measure symptom outcomes. On their own, these small studies represent a high risk of bias, but this is mitigated by the consistency of results they share with other more rigorous studies in the group. A meta-analysis was not performed due to the heterogenous nature of both the interventions and measured outcomes.

Theoretical Framework

Few investigators described formal theoretical models to support their hypotheses; 4 suggested theories of the Environment (including Nightingale's) as a framework for exploring the mechanism by which RMLI may affect patients in critical care (49-52) and 3 others proposed a cognitive neuroscience theory of meaningful stimulation (Table 2.3). 'Distraction' (48, 53, 54) and 'entrainment' (55, 56) were suggested by 5 study authors as a means to support the mechanism of music-induced symptom relief, and one group discussed a theory of Holism (57). The majority of studies discussed psychophysical or psychoneurological models wherein music stimulates the hypothalamic-pituitary axis and limbic system to change overall symptom state, however these mechanistic explanations were mooted as hypothetical models, not as tested theories (51, 58-65).

Study and Sample Characteristics

All reviewed studies were clinical trials with convenience samples (Table 2.3). Twenty-four used randomized designs and 6 were cross-over trials (49, 52, 58, 63, 64, 66). Studies were conducted in 11 countries including Western Europe (49, 51, 54, 61, 62, 65-69), the Middle East (57, 70, 71), Asia (47, 48, 52, 53, 56, 64) and North America (50, 55, 58-60, 63, 72-74). A total of 1717 participants were included. Study size ranged from 6-373 participants. The mean age of participants ranged from 34-74 years (mean 65.14 years) and 47.2% (n=811) were female sex. Race and ethnicity were reported in 5 studies (55, 59, 63, 72, 73), all of which were conducted in the US where most participants were white (84.6%). Participants were described as clinically stable and were enrolled between 1 to 16 days after admission. The majority of patients were described as 'awake', 'co-operative' or able to 'respond'; many studies stipulated the exclusion of any patients receiving continuous sedation. Only one study included agitated patients (52) and 7 included patients with decreased level of consciousness or who were chemically sedated (49, 50, 58, 60, 62, 70, 72, 74). Though most inclusion criteria stipulated broad descriptions such as 'stable ventilator settings,' or 'self-triggering modes,' specific ventilator settings at the time of enrollment were only described in 14 studies, and only 7 of these included spontaneous breathing modes (52, 54, 56, 62, 63, 68, 69).

Recorded Music Listening Intervention

Participants (or their surrogates) were offered a choice of music styles *from a limited selection list* of Western or Chinese classical, country, jazz, 'oldies', Chinese traditional, new age, religious music or movie scores in 11 studies (47, 48, 50, 53, 55, 56, 59, 64, 68, 71, 72) (Table 2.4). Three study investigators offered patient preferred music with restrictions on tempo and mood (described as 'relaxing') (63, 66, 73). Two study designs used unrestricted choice of any

music (52, 69). The remaining 11 studies used music selected by investigators: Western Classical music (51, 54, 58, 60-62, 74); Sufi compositions (65, 67); 'New Age' music (49); or instrumental music (70). Most music selections were described as 'relaxing,' and of a 'slow rhythm' often limited to 60-80 beats/min; however, one group included faster tempo pop songs (52). All but 2 of the included studies used headphones for music delivery: two studies used a pillow with embedded speakers (audio pillow) (65, 67). Participants listened to music for a fixed period of time, ranging from 20 min to 240 minutes, in all but one study where RMLIs were patient-initiated and the mean listening time was 79.8 minutes/day (72). RMLIs were delivered once (48-52, 54-56, 59-61, 64-67, 71), twice in one day (57, 58, 73), 3 times in 12-hour intervals (68) or daily over the length of the study period (49, 57, 62, 63, 69). Time of day of RMLI varied with many protocols using morning (9:00 or 10:00 am), evening (20:00) or in between. Four studies paired the RMLI with a painful event (endotracheal suctioning or turning) (62, 65, 67, 71), three were coordinated with a daily ventilator weaning trial (52, 63, 66), and two were coordinated with a daily sedation interruption (60, 74).

Control or Comparator Conditions

In 10 studies the control condition was a period of resting quietly with noise cancellation headphones (48, 49, 53, 56, 58, 60, 61, 69, 71, 72). One group used stereo headphones without noise cancellation (74) and 4 included a third condition of resting quietly *without* headphones (53, 61, 69, 72). Two studies compared patient-selected music to investigator-selected music (52, 73). Two studies did not describe the type of control condition used (54, 63). The remaining studies compared a music listening intervention to a period of controlled rest, or usual care without noise cancellation.

Symptoms Measured

The most commonly measured symptom was anxiety (48, 50, 52, 53, 55, 56, 63, 64, 68, 72, 73) (Table 2.5). The effects of music on sedation-agitation were explored in 11 studies (49, 51, 52, 55, 57, 58, 64, 66, 72-74). Procedural pain outcomes were measured in 4 studies (54, 62, 65, 67) and 4 explored pain outcomes more generally (49, 66, 70, 71). Stress was measured in 6 studies (48, 53, 58-61) and delirium in 2 (57, 73). Four studies considered outcomes of dyspnea or ventilator tolerance (49, 50, 63, 69). One study measured distress (69). No studies measured outcomes of sleep disturbances, loneliness, or fear.

Measurements of Symptom Experience

RMLIs were associated with deeper states of sedation when measured with Ramsay and Richmond Agitation Sedation Scores (RASS) in 5 of the 8 studies that used these instruments (52, 60, 65, 66, 68). Subjective report of anxiety, as measured by VAS and STAI, were lower after an RMLI in 7 of 10 studies (48, 50, 52, 53, 55, 64, 72). RMLIs were also associated with lower CPOT and Behavioral Pain Scores (BPS) in 5 of 7 studies that included these observed measures of pain (62, 65, 67, 70, 71). Self-reported pain was also significantly lower in the music condition in the only study that compared results of the NRS (66). Of the 2 studies that measured the symptom of dyspnea, only one noted a significant reduction in VAS of this symptom following an RMLI (63). Participants in the music arm also reported significantly reduced distress using the peri-traumatic distress inventory (PDI) in the only study to measure this symptom (49). Delirium, measured as proportion of time spent with a positive Confusion Assessment Measure for ICU (CAM-ICU) or as incidence of CAM positive, was not different between music groups and controls (57, 73). Seven studies reported qualitative findings including appearances of ‘calm’,

'restful' behaviors, falling asleep during RMLIs, reductions in 'agitated' behaviors, and subjective reports of feeling 'normal' and 'calm' (48, 49, 52, 60, 66, 72, 73).

Physiological Parameters

Hemodynamic parameters including HR, BP, RR, and other measures of breathing were measured in all but seven studies (50, 52, 64, 67, 70-72) (Table 2.5). Mean HR was decreased after listening to music in 6 studies (48, 53, 55, 56, 63, 66), but did not vary compared to a control condition in the other 10 studies that reported on this measure (49, 51, 57-62, 65, 68). Results were varied for the BP parameter assessed as: systolic (SBP), diastolic (DBP), and mean (MAP). Sixteen investigators measured SBP, but only 6 found a mean decrease in SBP associated with an RML (48, 51, 53, 54, 60, 66). Of the 12 studies that included DBP measurements, only 3 (51, 53, 54) showed a reduction after RMLIs, and MAP was reduced in only one study (48) out of the 6 which included this outcome measure. Six studies measured oxygen saturation (51, 53, 54, 61, 65, 69) but none found any statistically significant change after the RMLI. Mean RR was assessed in 16 studies and 6 showed reductions after RMLIs (53-56, 63, 66). Paired with this finding, data from one study demonstrated an increase in tidal volume and minute ventilation after an RMLI, compared to no change in the same parameters in the control arm (66). RMLIs were associated with a reduction in MV length in 2 trials (50, 57) and an increase in tolerance (time) of ventilator weaning trials in a third (63). Electroencephalogram recordings were not different after music compared to control in a single study (60) and Bispectral Index of Sedation (BIS) was lower after an RMLI in one study (66), but was unchanged in a second (49).

Serum biomarkers commonly associated with stress states were measured in 4 studies with mixed results. One group found that levels of Interleuken-6 (IL-6) and epinephrine decreased and levels of growth hormone increased after a 60-minute music listening intervention (60). But there

was no difference in IL-6 levels after an RMLI in Beaulieu-Boire, et al.'s cross over design study (58). Adrenocorticotrophic hormone (ACTH) and prolactin decreased significantly after the music listening intervention in one study (58) but were unchanged in another (60). Cortisol was reduced significantly in two studies (48, 58) but was unchanged in a third (59). Leptin, enkephalin (58), epinephrine (59) and norepinephrine (59, 60) were unchanged by music listening.

Medication Use

RMLIs were not associated with reductions in opioid (57, 58, 61, 72, 73), anxiolytic, sedative, or hypnotic use (58, 61). One group of investigators combined all hypnotic, opiate, and anxiolytic medications into a unique 'frequency of use' measure and an overall 'concentration of dose' measure and reported a statistically significant reduction of each in the music listening arm as compared to the usual care arm (72). Two groups found improved tolerance of sedation weaning with RMLIs compared to without (60, 74).

Discussion

To our knowledge, this is the first systematic review to report on the current uses of and effect of RMLI on commonly experienced symptoms in MV adults. This study supports prior research that has identified a benefit of MBIs for self-reported pain (39) in critically ill adults, and for self-reported anxiety in MV adults (42). New study findings show that RMLIs appear effective for use during procedural pain and ventilator or sedation weaning. This review also identifies several new uses of RMLIs for symptom management in MV adults to include relief of dyspnea, delirium, agitation, and distress. Methodological weakness and heterogeneity of outcome measures limit our ability to draw firm conclusions, but together these results provide preliminary evidence to support the use of RMLIs as an adjunct to symptom management in MV adults.

Symptom Measurement

In general, when symptoms were measured with validated scales or psychometric instruments such as the VAS, RASS, and CPOT, RMLIs were associated with improved symptom experience (dyspnea, pain, anxiety, agitation, and overall distress), whereas studies that relied on physiological variables failed to demonstrate an effect. We speculate that these lack of findings are because common physiological measurements lack specificity for symptoms experienced in critical care (75). In fact, none of the validated reliable tools used to measure pain, sedation-agitation, or delirium in critical care utilize HR, BP or RR in their construct; rather they are based on clinical judgment of the level of arousal, restlessness, facial expressions, body movements, executive function and responsiveness (76, 77). Some researchers have suggested entrainment as a theoretical model for the mechanism of action of music as a sedative which has informed the selection of relaxing music with a slower rhythm (60-80 beats/min) (78). However, this theoretical mechanism has not been demonstrated in critical care; noted reductions in mean HR after RMLI are likely coincidental (79). Mean HR may be affected by intravascular volume status, catecholamine agonist or antagonist medications, temperature, or a host of other confounding variables present in critically ill patients. Slower, deeper breaths have been associated with relaxation in healthy populations (80), thus change in RR can be conceptualized as a biomarker for change in somatic state. However, variance of RR is limited by pre-determined ventilator settings during MV. Similarly, listening to music has been associated with reductions in expression of stress hormones in healthy controls (81), but cortisol generally has poor specificity in critical care (82) and adrenal responsiveness, as well as cortisol metabolism may be blunted in critically ill adults (83, 84). Most importantly, physiological variables may sometimes demonstrate statistical significance, but, on their own, may not represent a meaningful clinical

outcome. As such, the use of these measurements does not advance our understanding of the effectiveness of RMLIs for symptom management.

The use of validated measures of symptom experience are a strength in several reviewed studies. Guidelines for the management of pain, anxiety/agitation, delirium and sleep include titration of medications against validated psychometric scales in patients unable to self-report, a practice that has been effective in reducing total sedative burden, length of MV and improving pain (13, 28). While not amenable to synthesis, the inclusion of other clinically meaningful outcomes, such as tolerance of sedation and ventilator weaning, and reduction in medication administration, also add to the strength of this review. The COMET (Core Outcome Measures in Effectiveness Trials) Initiative is a best practice collaboration endorsed by the Cochrane group that calls for the use of standardized, clinically meaningful outcomes, called core outcome sets, in all clinical trials (85). Benefits of the use of core outcome sets include reduction in reporting bias and an increased prospect of generating useful results.

Symptom Measurement in the Less Awake and During MV

Studies that gauge the effectiveness of RMLI against reliable measurements of symptoms, also allow for inclusion of less awake, more agitated, or more deeply sedated patients, a factor that will expand the potential applications for treatment with music in critical care. Until there are established core outcome measures for the effects of RMLI on common symptoms in critical care, the use of validated instruments such as the VAS scales (anxiety, pain, dyspnea) and psychometric scales such as the RASS, CPOT, BPS, Ramsey, and CAM-ICU contribute to the reliability and validity of future studies. Use of validated tools such as the Hospital Anxiety Depression Scale (HADS) and the peritraumatic distress inventory (PDI) by Messika et al (69) also represent important methodological advances for establishing a more complete understanding

of the potential benefits of RMLI while MV. Observations of patients smiling, seeming 'happy', tapping their feet, mouthing words, as well as reports that music made them feel 'normal' support this hypothesis (52, 72, 73).

Symptom Measurement of Sleep Quality

Lastly, we note the lack of studies examining the effects of RMLI on sleep quality in MV adults. Listening to music is associated with improved sleep in healthy adults (86) and there is evidence that listening to recorded music alone or alongside other mind-body interventions is associated with improved quality and quantity of restful sleep in *non* MV critically ill adults (87, 88). This is consistent with qualitative observations in several of the reviewed studies. Given the importance of adequate sleep, both for symptom experience and prevention of delirium, studies that use validated instruments to examine the use of music to treat and prevent sleep disorders represent an important area for future research.

Other Symptom Measurement Factors

Overall, this review includes 1717 patients on 3 continents, adding to the generalizability of the findings. However, results of the reviewed studies may have been influenced by the older mean age of the cohort age (>65). Older age is a risk factor for delirium and is associated with decreased metabolism of sedative and analgesic medications that can influence symptom outcomes (8). Several studies stipulated an awake, interactive state as inclusion criteria in their designs, but few included a formal screen for delirium. If present, delirium may have affected the results as hypoactive delirium can dampen a patient's arousal and hyperactive delirium may result in increased use of restraints, antipsychotics or sedatives to maintain patient safety.

Variable symptom experience within individuals may also have affected the results. Most studies measured the outcome of only one symptom and did not account for the potential

interaction of a co-occurring symptom. This was most common with studies of anxiety and pain, two independent symptoms that are known to interact (89, 90). None of these potential confounds diminish the self-reported improvements in symptoms, but they do limit the strength of our ability to infer causal relationships between RMLI and specific symptoms. Disparate medication administration also may also have biased the results of the studies. For example, sedative use is associated with reduction in analgesia (91). Lack of formal medication administration protocols also threaten the reliability of symptom outcome studies. This approach is problematic as the absence of an agreed upon goal or target sedative level may result in disparate sedative administration (77). Studies that include an RMLI within a protocol-based medication plan may help clarify the potential for RMLI to reduce or replace sedatives in critical care.

Music Selections

It is difficult to know what role music selection played in the symptom outcomes. Despite recommendations to tailor music selections to patient preference (92-97) most of the studies limited choice of music (n=22) to 'traditional', 'instrumental', or Western classical music. However, patients in US-based studies have also identified jazz, country, pop music, rock and roll, and spiritual music as 'preferred', 'relaxing', and helpful for pain control (98). Even when choice was offered, selection was usually limited to slow tempo 'relaxing' music, or to a choice between a group of investigator-selected playlists. Yet studies of people with altered consciousness suggest that compared to 'relaxing classical' or investigator chosen 'neutral' music, *use of preferred music, regardless of tempo,* is associated with a stronger effect demonstrated by greater reduction in agitation after traumatic brain injury (99), improved level of consciousness after coma (100), or increased relaxation response in the operating room while under light anesthesia (101). Listening to a preferred musical genre or familiar music has been

associated with increased relaxation effect and heightened pleasure arousal in healthy adults (102, 103). While it is not clear if this finding translates to the critically ill patient population, offering a patient-centered and patient-selected music may confer increased benefit of an RMLI. In fact, the 3 studies which offered an unlimited personalized selection of music demonstrated a statistically significant relaxation effect (52, 63, 66).

Newer technologies such as tablets and music streaming services afford increased access to unrestricted music of choice. Family members and close acquaintances may know best what music is most helpful to individuals unable to self-report in the ICU since the basis of our musical preferences is rooted in our socio-cultural context (104). Additionally, family and friends may be more reliable assessors of symptoms experienced by ICU patients than clinicians (105). Culturally humble care which is informed by cultural identity, personal preferences, history, and context may help to reduce health inequities and restore health after injury (106).

Delivery of Music Interventions

Variations in the control arms and the potential therapeutic effect of noise cancellation headphones may have reduced the strength of the findings. Critical care units are plagued by high noise levels and the World Health Organization has made recommendations to offer earplugs or headphones to reduce this (107, 108). Additionally, headphones themselves have been studied for promotion of sleep and prevention of delirium (25, 109). Maintaining headphone use across both arms attends to concerns of internal validity. Conversely, the use of headphones may add to feelings of disconnectedness, communication barriers, and feeling de-situated especially during MV. Studies which explore the use of music delivered ambiently may suffer methodological criticism but may be more pragmatic and acceptable.

Music Intervention Protocols

The heterogeneity of duration, timing and frequency of RMLIs in these studies precludes any summary conclusions about optimal length or frequency of RMLIs; however, the wide variety of symptoms included in this broad review likely require varied management approaches. Results of the studies in this review suggest that coordinating RMLI alongside a stressful stimulus may increase be of benefit. Some symptoms are brief and related to a specific stimulus or stressor, such as procedural pain. Research exploring cognitive processing of music suggests that adults are affected by listening to music within minutes (110, 111) and that RMLIs of short durations (10-15 minutes) are associated with improved level of arousal during coma recovery (112, 113). This rapid onset of effect may help explain the why short RMLIs (20-30 min) were effective for management of procedural pain in the studies in this review. However, longer RMLIs were also well tolerated when administered during ventilator and sedative weaning. Planned sedation interruptions, called 'daily wake up' periods, are the standard of care to promote early weaning from MV and reduction of sedative use (114). Studies exploring the effects of RMLI during general anesthesia indicate that RMLI are associated with reduced emergence delirium and increased satisfaction compared to controls (115). Though sedative medication requirement was not formally assessed as an outcome in the studies that examined people during sedation interruption or emerging from anesthesia, the authors observed that patients who received an RMLI required less rescue sedative compared to patients in the control conditions. Similarly, patients who received an RMLI intervention *during* and immediately after surgery with general anesthesia experienced a subjective reduction in anxiety state (50). Other symptoms, such as sleep disruptions, are related to time of day and others, such as anxiety, may wax and wane (116). This highlights an important area of research in therapeutic RMLIs for critically ill patients: optimal

frequency length and duration of effect of RMLIs, though this is likely to depend on the symptom of interest.

Limitations

This review was limited to published peer reviewed journals and may be affected by publication biases (117). Two grey literature citations appeared to meet inclusion criteria but were unpublished data. Other relevant citations were only available as conference abstracts, with limited data on methods and results and were therefore excluded. A second limitation of this review is that the search was limited to publications in English and French; at least 4 other studies met inclusion criteria but were published in Korean, Greek, Spanish and Chinese, and therefore were not incorporated. Finally, this review does not include meta-analysis due to the heterogeneity of outcome measures, a result of the broad scope of this review.

Conclusions

These 28 studies add to prior research that demonstrates improved self-reported symptom experience associated with RMLIs in awake, responsive MV adults. Additionally, changes in observed pain, agitation, sedation level, and ventilator tolerance were appreciated in adults unable to self-report due to altered levels of consciousness. Unlike prior reviews, listening to music was not associated with changes in vital signs. Instead, the use of validated psychometric instruments provided evidence of the effect of music on symptoms of pain, anxiety, agitation, dyspnea, and distress. There remain substantial expansion opportunities for RMLIs use among MV adults to include testing the effects of varied types of music and expanding the outcomes of interest to incorporate measures of sleep quality, psychological wellbeing, and ventilator tolerance. Future clinical trials that seek to maximize potential therapeutic benefit of an RMLI in MV will benefit

from research that identifies reliable, meaningful measures and that help explain the underlying mechanism of action of music intervention.

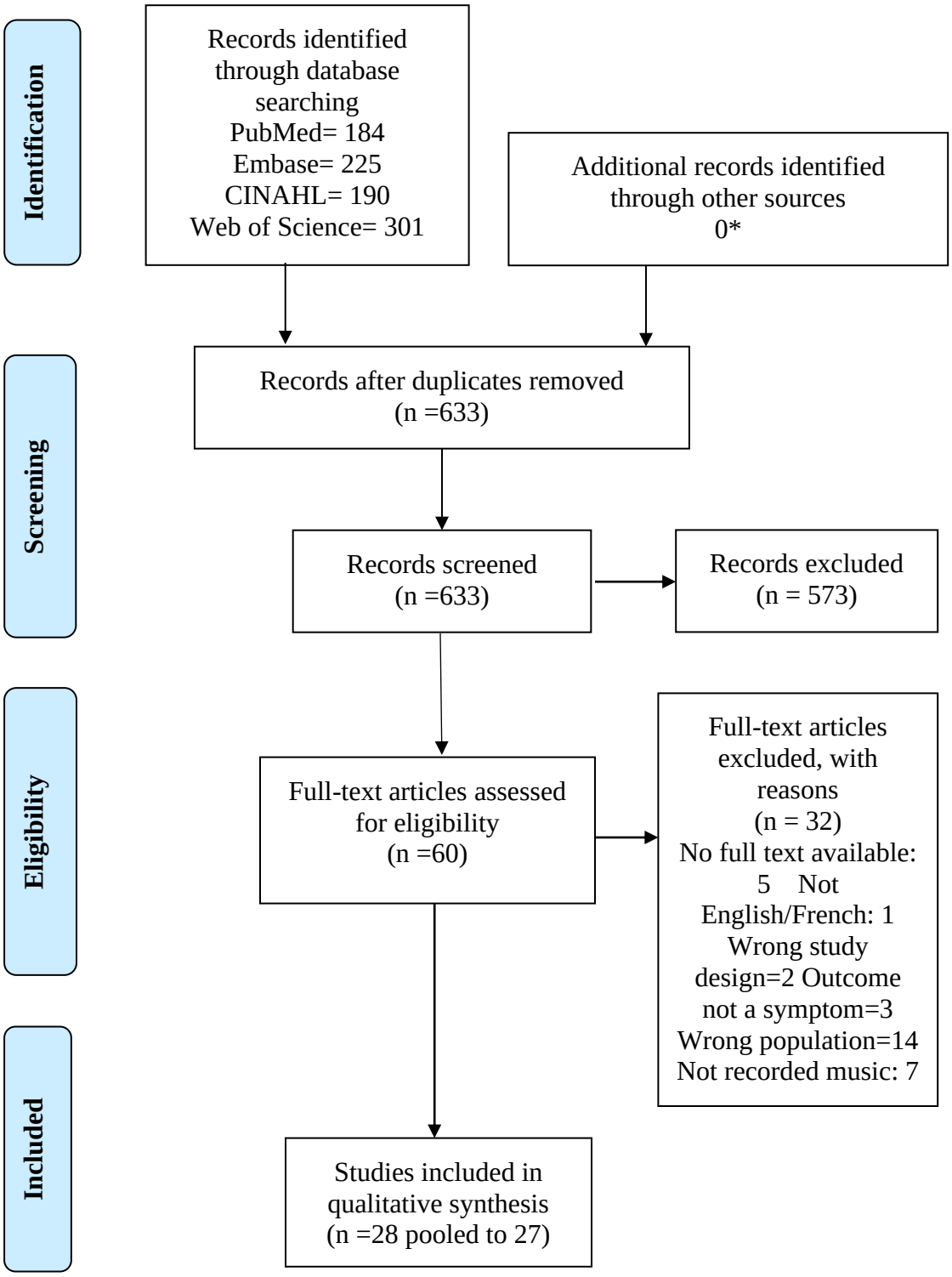


Figure 2.1: **PRISMA Flow Diagram**

Table 2.1: **Inclusion and Exclusion Criteria**

	INCLUDED	EXCLUDED
POPULATION	Adults >17 yrs. old Mechanically Ventilated	Neonates, Children (<18), Breast Feeding Mothers, Mothers of Neonates, Burns
INTERVENTION	Recorded Music Listening Intervention	Live Music, Music Bundled with other Complementary Health Interventions, 'No Music'
CONTROL	Placebo, or "no music"	
SETTING	Surgical or Medical Intensive Care Unit (ICU)	Procedural Suites, Operating Room, Recovery Room
DESIGN	Experimental Designs, Randomized Controlled Trials, Quasi-Experimental Trials, Clinical Trials, Cross-Over	Qualitative, Commentary, Reviews, Protocols, Editorials, Cost Effectiveness Trials
OUTCOME of MEASURE	Pain, anxiety, agitation, dyspnea, shortness of breath, sedation, ventilator tolerance, sedative, loneliness, delirium, confusion, stress, insomnia, sleep, fear, satisfaction, depression	Not a measure of a symptom (e.g., feasibility, demographics)
DATES	January 1, 1998, and March 20, 2022	Prior to January 1, 1998, After March 20, 2022
LANGUAGE	English or French	Not in English or French

Table 2.2: Quality of Evidence Using the Evidence Project Risk of Bias Tool

First Author, Publication Year	Cohort	Control Comparator	Pre-Post	Random Assignment	Random Selection	Follow Up >80%	Social Clinical Equal	Baseline outcomes Equal	total
Aktas, 2015	Y	Y	Y	Y	N	Y	Y	Y	7
Aktas, 2018	Y	Y	Y	Y	N	Y	Y	Y	7
Almerud, 2002	Y	Y	Y	NR	N	Y	Y	NR	5
Beaulieu-Boire, 2013	Y	Y	Y	Y	N	Y	Y*	Y**	7
Chlan, 1998	Y	Y	Y	Y	N	Y	Y	Y	7
Chlan, 2007	Y	Y	Y	Y	N	Y	Y	Y**	7
Chlan, 2013	Y	Y	Y	Y	N	N	N	N	4
Conrad, 2007	Y	Y	Y	Y	Y	Y	Y	NR	7
Damshens, 2018	Y	Y	N	Y	N	Y	Y	NR	5
Dijkstra, 2010	Y	Y	Y	Y	N	Y	Y	Y	7
Han, 2010	Y	Y	Y	Y	N	Y	Y	Y****	7
Iblher, 2011	Y	Y	Y	Y	N	N	Y	Y	6
Jaber, 2006	Y	Y	Y	Y	N	Y	Y	Y	7
Jacq, 2018	Y	Y	Y	N	N	Y	Y	Y	6
Khan,2020	Y	Y	N	Y	N	N	Y	NA	4
Korhan, 2011	Y	Y	Y	Y	N	NR	NR	Y	5
Kyavar, 2016	Y	Y	Y	Y	N	NR	Y	Y	6
Lee, 2017 ****	Y	Y	Y	Y	N	Y	Y	Y	7
Lee, 2005	Y	Y	Y	Y	N	NR	Y	Y****	6
Liang, 2016	Y	Y	Y	Y	N	N	Y	Y	6
Mateu-Capell, 2018	Y	Y	Y	Y	N	Y	Y	Y	7
Messika, 2019	Y	Y	Y	Y	N	N	Y*****	NR	5
Park, 2019	Y	Y	Y	NA	N	Y	Y	NR	5
To, 2013	Y	Y	Y	Y	N	Y	Y	N	6
Twiss, 2006	Y	Y	Y	Y	N	N	Y	Y	6
Wong, 2001	Y	Y	Y	Y	N	Y	Y	Y	7
Yaghoubinia, 2016	Y	Y	Y	Y	N	Y	Y	N	6

Y = met, N = not met; NR: not reported, NA = not applicable
* = control group more sedatives; **= baseline cortisol differed between groups****= combined Lee et al papers for reporting (single cohort); *****= higher baseline carbon dioxide level in music group

Table 2.3: Study and Sample Characteristics

First Author, Title, Year, Country	Research Aims, Question Symptom of Interest	Study Design	Theoretical Framework	Sample Characteristics			
				Inclusion Criteria *(Exclusion Criteria)*	**Sample Size, Demographics**	**Clinical Phenotype**	**Ventilator mode, airway**
Aktas, 2015 The Effects of Music Therapy in Endotracheal Suctioning of Mechanically Ventilated Patients Turkey	To measure the effect of music 'therapy' on **[procedural] pain, sedation level** during suctioning?	Randomized controlled, single blind experimental	Not Reported	Scheduled open heart surgery, age >17, intubated, requiring suctioning, **Ramsay Scale 2-3 at enrolment** *(ejection fraction ≤25%, unstable hemodynamics, requiring vasoactive support, neuromuscular blockade, chronic pain)*	N= 66 Age: 65 yrs. Female: 27% Primary School: 80% Married: 86% Ethnicity or Race: NR	ICU (CVICU) *Hours* of MV: Music: 3.81 Control: 4.28	Not Reported
Aktas, 2018 Relief of Procedural Pain in Critically Ill Patients by Music Therapy: A Randomized Controlled Trial Turkey	Does music lessen **procedural pain** during suctioning?	Randomized controlled trial	limbic system activation	Intubated, requiring suctioning, **Ramsay Scale 2-3 at enrollment** *(ejection fraction ≤25%, unstable hemodynamics, neuromuscular blockade, chronic pain medications,* any change in sedative or analgesia during trial*)*	N= 80 Age: 65.95 Female: 35% Primary School: 81% Married: 85% Ethnicity or Race: NR	CVICU *Hours* of MV: Music: 3.90 Control: 4.25	Not Reported
Almerud, 2002 Music Therapy- A Complimentary Treatment for Mechanically Ventilated Intensive Care Patients Sweden	Does music 'therapy' have a measurable **relaxing** effect on mechanically ventilated (MV) ICU patients?	Mixed method Experimental design With control condition	Environment (familiar sound, blocking noise) HPA/limbic	Adults requiring temporary MV, clinically 'stable' *(psychiatric condition, severe depression, developmental delay, intra-cranial hemorrhage)*	N=20 (10 in each arm) Women: 60% Age: 66.5 Ethnicity or Race: NR	Mixed ICU *Days* of MV: music 13.95 Control: 9.1 **RASS -1 to 0**	Not Reported
Beaulieu-Boire, 2013 Music and Biological Stress Dampening in Mechanically Ventilated Patients at the Intensive Care Unit Ward- A Prospective interventional Randomized Crossover Trial Canada	Does music augment **sedation** (↓sedative requirement); does music dampen **stress** response	Randomized controlled trial with crossover design	No formal model HPA axis mechanism	Age>17, **requiring sedation medication for Sedation-Agitation Scale (SAS) 3-4**, requiring ≥3 days MV, on 'self-triggering mode, stabilized overall medical condition *(deaf, pregnant, requiring SAS 1-2, neuromuscular blockade)*	N= 49 Age= 62 Female 31% Ethnicity or Race: NR	Medical ICU *Days* of MV days: 11.5 APACHE: 26 Equal adrenergic agonist and corticosteroid	Mode: self-triggering or 'weaning' mode Airway: Not Reported

First Author, Title, Year, Country	Research Aims, Question Symptom of Interest	Study Design	Theoretical Framework	Sample Characteristics			
				Inclusion Criteria ***(Exclusion Criteria)***	**Sample Size, Demographics**	**Clinical Phenotype**	**Ventilator mode, airway**
Chlan, 1998 Effectiveness of a Music Therapy Intervention on Relaxation and Anxiety for Patients Receiving Ventilatory Assistance USA	Is listening to music effective as a **relaxant** or an **anxiolytic** during MV?	Experimental Design with control group: 2 groups pre-test post test	Entrainment, synchronization of body rhythms, perceptual focus stimulation	Ventilator dependent, **alert**, mentally competent, not hearing impaired, primary English speaking, not receiving continuous sedation *(exclusion criteria not stated)*	N=54 Age: 57.1 [18, 89] Female: 59% Ethnicity or Race: White : 92% African American: 6% Native-American: 2%	3 Hospitals, 4 Mixed ICU *days* of MV:7.4 Music: ↑antiemetics, anti-histamine agonists, diuretics; Control: ↑ antidepressants	Mode: SIMV 70% PEEP: NR Airway: NR
Chlan, 2007 Influence of Music on the Stress Response in Patients Receiving Mechanical Ventilation USA	Does listening to music alter **stress** response	Quasi Experimental Design with control group Repeated measures	No formal model; reference HPA axis mechanism	Ventilator dependent, **alert**, central venous access, hemodynamically stable, intact renal function, not anemic, not receiving continuous sedation or steroids *(exclusion criteria not stated)*	N=10 Female: 60% Ethnicity or Race: White: 90% African American/Black: 10%	MICU *days* of MV: Music:15.5 Control:12.8	Mode: AC: 60% SIMV 20% Pressure Release 20% Airway: NR
Chlan, 2013 Effects of Patient Directed Music Intervention on Anxiety and Sedative Exposure in Critically Ill Patients Receiving Mechanical Ventilatory Support: A randomized clinical trial USA	Does listening to music reduce **anxiety** and **sedative** exposure?	Randomized Controlled trial: 3 groups: music listening, noise cancellation, usual care	Distraction, meaningful cognitive stimuli	Receiving MV, **alert**, cognitively intact, adequate corrected hearing/vision *('aggressive' MV support, requiring vasoactive medications, unresponsive, delirious, mental incompetence, prior chronic MV)*	N= 373 Mean Age: 59 Female: 52% Ethnicity or Race: White: 86%	12 ICUs in 5 hospitals *days* of MV music 4.5 noise cancel 6, usual care 6 APACHE III: 63	NR
Conrad, 2007 Overture for Growth Hormone: Requiem for Interleukin-6? USA	Does listening to [Mozart] music reduce **stress**?	Randomized Controlled Trial 2 arms: music and control	Novel model Proposed neurohumoral pathway (bidirectional) via HPA-axis)	Adults with an APACHE score > 16, intubated, post-operative, **sedated** with propofol *(exclusion criteria not stated)*	N = 10 Age: 52.9 (46-77) Female: 10% Ethnicity or Race: NR	All post-operative admitted to surgical intensive care (SICU) **Ramsay 1- 2**	NR

First Author, Title, Year, Country	Research Aims, Question Symptom of Interest	Study Design	Theoretical Framework	Sample Characteristics			
				Inclusion Criteria ***(Exclusion Criteria)***	**Sample Size, Demographics**	**Clinical Phenotype**	**Ventilator mode, airway**
Damshens, 2018 The Role of Music on The Delirium in Traumatic Patients: A Case Study of Peymanieh Hospital, Iran	Does listening to music result in decreased incidence of **delirium**, or **sedative** or **analgesic** medications	Controlled clinical trial	Not formally proposed Holism (harmony of mind and body)	Mechanical ventilation > 48 hrs., > 15 yrs. old, trauma service *(cognitive impairment, uncorrected visual/audio impairment, depression, prescribed psychotropic drugs, substance abuse)*	N= 80 Male: 95% Age 34.27 yrs. Ethnicity or Race: NR	ICU after trauma APACHE IV score: 32.89 Arousal level NR	NR
Dijkstra, 2010 The Effects of Music on Physiological Responses and Sedation Scores in Sedated, Mechanically Ventilated Patients Netherlands	Does listening to music when sedated and with MV result in deeper levels of **sedation** and lower [physiological signs of] ICU **anxiety**	Randomized Controlled Trial, with repeated measures 2 Arms: music and control	Not Reported	Mechanically ventilated, self-triggering mode, no hearing impairment, receiving **continuous sedation** with midazolam or propofol, and *(exclusion not specified)*	N= 20 Female: 40% Age: 52 Ethnicity or Race: NR	Mixed MICU and SICU ICU days at start: 6.8 No difference sedative dose **Ramsay score 3-4** **Sedic 5**	Mode: PS: 95% SIMV: 5% Airway: Not Reported
Han, 2010 Effects of Music Intervention on Physiological Stress Response and Anxiety Level of Mechanically Ventilated Patients in China China	Does listening to music reduce state **anxiety** and signs of **stress**	Randomized Controlled Trial 3 groups music, placebo (silence) and control	Distraction, Entrainment (bidirectional) Chinese Philosophy (music as 'celestial energy of perfect harmony'	Chinese, understand Mandarin, **alert**, mentally competent, able to communicate with hand gestures, **not receiving continuous analgesia/sedative**, no previous music intervention *(hearing impairment, skull injury preventing headphones, CMV or CPAP ventilation modes)*	N=137 Age 46.18 Female: 46% Primary School: 63.5% Ethnicity or Race: NR	Single Mixed ICU Arousal level NR	Mode: SIMV: 119 (87%) PCV: 18 (13%) Trach 11% PEEP: 2.3 FiO2: 40.46 Airway: ETT: 89%,
Iblher, 2011 Does Music Harm Patients after Cardiac Surgery: A Randomized Controlled Study Germany	Does a music intervention reduce physiological signs of **stress** or drug consumption (catecholamines or opioid **analgesics**)	Randomized controlled study 5 groups: sedative + music; sedative + noise cancel; music *after* sedative; noise cancel *after* sedative; usual care	No formal theory suggest music acting on HPA → *amygdala spinal cord neuron release of enkephalin; hippocampus stimulation*	Adults admitted to ICU immediately post operatively from elective cardiac surgery; **sedated with propofol or emerging from propofol sedation**. (*baseline high anxiety, psychological disorders, amblyacousia or expected prolonged recovery*)	N = 126 Age 66.9 yrs. Female: 21.4% Male: 78.6% Ethnicity or Race: NR	SICU Enrollment immediately post-operatively	Not Reported

First Author, Title, Year, Country	Research Aims, Question Symptom of Interest	Study Design	Theoretical Framework	Sample Characteristics			
				Inclusion Criteria ***(Exclusion Criteria)***	**Sample Size, Demographics**	**Clinical Phenotype**	**Ventilator mode, airway**
Jaber, 2006 Effects of Music Therapy in Intensive Care Unit without Sedation in Weaning Patients versus Non-Ventilated Patients France	What is the effect of a music intervention on hemodynamic and respiratory parameters, **pain** experience and **awake-vigilance state**?	Randomized Prospective Cross Over Observational (music vs rest)	Not Reported	Age > 18 Ability to follow simple commands PEEP </= 5 cm H2), pressure support </= 15 cm H20, FiO2</=50% ***(concomitant sedation** or vasoactive agents)*	N= 15 Age 58 +/- 9 Female: 7/15 Male 8/15 Ethnicity or Race: NR	Mixed ICU ICU *days* of MV: 12 Acute Physiology Score (IGS II): 39 **RASS -1 to +1**	Mode: PSV (12 cm H20) PEEP 4 cm H20 FiO2 42 Airway 13 ETT 2 Trach
Jacq, 2018 Music for Pain Relief During Bed Bathing of Mechanically Ventilated Patients: A Pilot Study France	What is the effect of music on **pain** during bed bath?	Experimental Design (non-randomized) 2 groups consecutive enrollment	No formal theory. Suggested mechanism HPA/limbic pathway, endorphin release mediates pain experience	Age >18 **RASS -3 to +4** Receiving MV *(receiving neuromuscular blocking agent, under guardianship, not insured in France, no family, co-enrollment in another study)*	N= 60 Age 69 [60, 80] Female: 49% (↑in music) Ethnicity or Race: NR	Mixed ICU *days* of MV: 5 Acute Physiology Score II: 55.75 Sedatives: 17/60 Analgesia: 14/60 **RASS 0**	Mode: AC: 5 PSV: 55 Airway Not Reported
Khan, 2020 Decreasing Delirium Through Music: A Randomized Pilot Trial USA	What is the effect of personalized or slow-tempo music on indices of **agitation**, **anxiety** and **delirium** in MV adults?	Randomized Controlled Trial	No formal theory	Receiving MV > 24 hrs., < 48 hrs. English Speaking *(chronic or severe acute neurological disorder/injury, uncorrected vision/hearing loss, intoxicated or experiencing withdrawal, pregnant/nursing, in custody, anoxic coma)*	N= 52 Age= 57.4 yrs. African American: 40% Female Sex: 52% High School: 42%	Mean APACHE score 21.7 **Arousal level NR**	Not Reported
Korhan, 2011 The Effect of Music Therapy on Physiological Signs of Anxiety in Patients Receiving Mechanical Ventilatory Support Turkey	What is the effect of classical music on physiological signs of **anxiety** in MV [Turkish] patients?	Randomized Controlled Trial (sub analysis responders as case control) 2 arms music intervention and control	No formal theory Suggested mechanism of distraction and repetitive behavior with effect on vital signs	Mechanically ventilated, able to hear**, GCS ≥ 9**, hemodynamically stable, adult (>18 yrs.) *(excluded: psychiatric/ neurological illness, inotropic support, no neuromuscular blocker, no anti-hypertensive Rx)*	N = 60 Age: 45 (18-70) Female: 28/70 Ethnicity NR Education level: 33 primary 16 secondary 11 tertiary	MICU Day of MV: 8 ns **Arousal level NR**	Mode: PSV FiO2 </= 0.4 PEEP </=6, PS adjusted to goal TV 6-8ml/kg

First Author, Title, Year, Country	Research Aims, Question Symptom of Interest	Study Design	Theoretical Framework	Sample Characteristics			
				Inclusion Criteria ***(Exclusion Criteria)***	**Sample Size, Demographics**	**Clinical Phenotype**	**Ventilator mode, airway**
Kyavar, 2016 Effect of preferred music listening on pain reduction in mechanically ventilated patients after coronary artery bypass graft surgery Iran	Does listening to preferred music reduce **pain** after CABG in MV adults?	Clinical Trial (single blind) Randomization not described	Not Reported, *suggest music influence over immune system, personal preference and context enhance effect*	Age >18, MV after elective CABG with sternotomy, Unable to communicate verbally, no facial injury, first time admission to SICU, stable hemodynamically: HR 60-120 bpm, SBP>90 mmHg, **awake from anesthesia**, hearing intact *(quadriplegia, continuous use of sedative, analgesic or muscle relaxant during study period, cardiopulmonary arrest during OR, history of chronic pain)*	N=60 Age: 60.2, Female 22% Ethnicity NR Married: 90%, Retired: 42%, Employed: 58%, Smoking: 43%, Opium use: 25%, Music Listening Everyday: 5% Sometimes: 45% Occasion/Rarely: 47% Never: 3%	Cardiac Surgery ICU *Hours* on MV: 3-5 hours **RASS -3 - +2** sedatives: 7/60 analgesia: 6/60	Mode: Not Reported ETT 100%
Lee, 2017 Effects of Music Intervention on State Anxiety and Physiological Indices in Patients Undergoing Mechanical Ventilation in the Intensive Care Unit: A Randomized Controlled Trial ** China	Does listening to music reduce **anxiety** in MV ICU patients?	Randomized Controlled Trial: 2 groups Random number list Excel	Distraction, Entrainment and Pleasure invoking limbic activation	Age 18-85, **conscious, mental clarity to participate and understand**, Mandarin or Taiwanese speaking, able to communicate using gestures, ICU admit>1 day (*hemodynamic instability, continuous analgesia/sedatives, treated with steroids, impaired hearing, skull injury, infectious disease, alcoholism, use of restraints*)	N= 85 Age: 59.33 yrs. Female: 56% Ethnicity or Race: NR Highest Education: Primary School: 36% High School: 15% College or more: 49% Religion (yes): 55% Married: 59%	Mixed ICU Length of MV days: 2.54	PACV 41 PS 32 AC 12 Airway: ETT: 70 Trach 15
Lee, 2005 Music and Its Effects on the Physiological Responses and Anxiety Levels of Patients Receiving Mechanical Ventilation China	Does music affect Chinese **state anxiety** scores, does music lower physiologic vital signs (associated with **stress**)?	Randomized Controlled Trial 2 groups Music and control (group assignment by lot draw)	Entrainment with subsequent activation of sympathetic and autonomic nervous systems	**Alert**, no psychiatric illness, able to follow simple commands, hearing intact, hemodynamically stable, self-triggering mode on MV (*hemodynamically unstable*)	N=64 Age: 69.4 Female: 28.1% Ethnicity or Rave: NR NOT religious 76%. Education Level: Primary Education or Less: 83% Unemployed: 84%	Mixed ICU Length of MV: NR	Mode: SIMV 1 PS 57 Settings: PEEP 5.4 PS 9.8, FiO2 37.7% Airway: ETT: 58 Trach 3 Nasal 3

First Author, Title, Year, Country	Research Aims, Question Symptom of Interest	Study Design	Theoretical Framework	Sample Characteristics			
				Inclusion Criteria ***(Exclusion Criteria)***	**Sample Size, Demographics**	**Clinical Phenotype**	**Ventilator mode, airway**
Liang, 2016 Music Intervention During Daily Weaning Trials- a 6-day Prospective Randomized Crossover Trial USA	Does listening to music lessen **anxiety** and **dyspnea** during weaning from MV?	Randomized Cross Over Design (randomization via note card selection)	Psychophysiological weaning model and distraction or? activation of limbic by music (no formal mechanism)	Age>20 yrs. old, on MV >3days, tracheostomy, **NOT delirious** (**CAM-**, RASS), undergoing daily weaning, able to use headphones to hear music *(exclusion not specified)*	N= 23 Age: 61.6 +/- 10.9 Female: 6 (27.1%) Ethnicity or Race: White: 22 (95.7%)	Prolonged MV Weaning Unit Length of MV: NR APACHE III: 48.4n.s.	Not Reported described as 'weaning mode' Airway: Trach: 23 100%
Mateu-Capell, 2018 Sound Isolation and Music on the Comfort of Mechanically Ventilated Critical Patients Spain	Does music (or sound isolation) increase **comfort**, **sedation** or **pain** (**ventilator tolerance**) in MV patients?	Randomized Controlled Trial with Crossover 2 arms (computer generated random sequence)	Environment	Age >18, **Bispectral Index of Sedation (BIS) ≥50, receiving any type of sedation** *(limited resuscitation orders in place, temperature >37.5 C, hearing impaired, severe mental health disorder, acute disorder of central nervous system)*	N=75 Age: 68.06 Female: 20 (27%) Ethnicity or Race: NR Education Level: NR Companion/Family: 48 (64%)	ICU days: 8-9 BIS: 70.56, Sedatives: 76% Vasoactives: 64% **Anxious or Agitated: 8%** **Calm: 14.7%** **Response to Stim:** **Verbal: 8%** **Brisk: 10.6%** **Sluggish: 28%** **No Ree: 30.6%**	Length of MV days: 1-4 AC: 54 PSV: 12 PAV: 9 FiO2 33%,
Messika, 2019 A Musical Intervention for Respiratory Comfort during Noninvasive ventilation in the ICU France	What is the effect of preferred music on **respiratory discomfort**, **tolerance of noninvasive mechanical ventilation** (NIMV) and **PTSD** symptoms	Randomized Controlled Trial	No formal theoretical framework	Age > 18yrs, acute respiratory failure, GCS >/= 12, assessed as needing NIMV *(severe hearing impairment, anticipated life expectancy <48 hrs., or co-enrollment in another respiratory study)*	N = 113 Age: 66 [57, 76] Female: 55% Ethnicity or Race: NR Baseline psychiatric, anxiety and depression equal across groups	Comorbid clinical Conditions and indications for NIMV Equal Across Groups Acute on Chronic Failure: 54% Arousal Level NR	Duration of respiratory failure not reported NIMV for all settings NR

First Author, Title, Year, Country	Research Aims, Question Symptom of Interest	Study Design	Theoretical Framework	Sample Characteristics			
				Inclusion Criteria ***(Exclusion Criteria)***	**Sample Size, Demographics**	**Clinical Phenotype**	**Ventilator mode, airway**
Park, 2019 Effects of Two Music Therapy Methods on Agitation and Anxiety among Patients Weaning off Mechanical Ventilation: A Pilot Study Korea	What is the effect of preferred or classical music on **agitation** and **anxiety** during MV weaning?	Randomized Clinical Trial Cross Over Design	Environment	Age >18, pressure support ventilation mode, alert/communicative, hemodynamically stable, PaO2/FiO2 >200, HR <140 bpm, MAP >60 mmHg, able to use headphones *(psychiatric illness, cognitive disorders, receiving continuous parenteral sedation, neurological disorders)*	N=6 Age: 45.33 yrs. Female: 66% Ethnicity or Race: NR	Mixed medical surgical diagnoses **RASS +1** *days* of MV: 10.67	PSV: all (specific parameters NR)
To, 2013 Mozart Piano Sonatas as an Adjunct to Facilitate Sedation Vacation in Critically Ill Patients Canada	Does music reduce requirement of **sedation** during MV	Randomized Clinical Trial	Not reported	Receiving MV, **sedated with propofol and or midazolam**, eligible for daily sedation interruption (*implanted device, deaf, ear or scalp injury, neuromuscular blockade, advanced ventilation technique, acute events prior 24 hours, elevated ICP, benzodiazepine or alcohol dependence, long term opioid use*)	N= 50 Age= 50.4 yrs. Female: 27% Ethnicity or Race: NR	Mixed trauma (42%), medical, neurosurgical and surgical ICU **Baseline Ramsay 3-4**	Not Reported
Twiss, 2006. The Effects of Music Listening on Older Adults Undergoing Cardiovascular Surgery USA	Does music effect post-operative **anxiety** or length of MV after CABG or Valve surgery?	Randomized Clinical Trial: Exploratory	Nightingale Environment	Age >65 yrs., oriented to person, time, place at admission; not currently using music therapy, intact hearing, able to complete pre-trial STAI screen *(exclusion not specified)*	N= 60 Age: 73.88, Female: 67%, Ethnicity or Race: NR	CVICU **Waking from sedation** Baseline STAI: 44.5 ns	Not Reported
Wong, 2001 Effects of Music Therapy on Anxiety in Ventilator-Dependent Patients China	Does listening to music lessen **anxiety** or promote **relaxation** in MV adults?	Randomized Controlled Trial with Crossover 2 arms	Suggested mechanism physiological psychological integration; promote wellbeing/health, mood alteration	Chinese, understand Cantonese or English, age 18-85, **alert**, mentally competent, intact hearing, MV with self-triggering mode, able to communicate with gestures, hemodynamically stable (no inotropic support), not previously enrolled in music trial *(exclusion not specified)*	N= 20 Age: 58.25 yrs. Female: 25% Ethnicity or Race: NR Married: 18 (90%) No Religion: 12 (60%) None/Primary School:75% Employed: 10	Mixed ICU *days* of MV: 6.05 STAI: 52.88	"Self-trigger" PSV:=16 SIMV: n=4 Pressure: 8-20 PEEP: 3-12 FiO2: 0.3-0.6 ETT: 8, Trach: 12

First Author, Title, Year, Country	Research Aims, Question Symptom of Interest	Study Design	Theoretical Framework	Sample Characteristics			
				Inclusion Criteria ***(Exclusion Criteria)***	**Sample Size, Demographics**	**Clinical Phenotype**	**Ventilator mode, airway**
Yaghoubinia, 2016 Effect of music therapy and reflexology on pain in unconscious patients: A randomized clinical trial Iran	Does listening to music reduce **pain** score in MV adults?	Randomized Controlled Trial 3 arms (usual care, music and reflexology) 'researcher assigned randomization'	Not Reported	Non traumatically injured **Altered Level of Consciousness (GCS 5-8),** hearing intact, receiving IV fentanyl 25-50 µ infusion, first time ICU admission, healthy feet *(alcohol/drug/cigarette addiction, extubation or regain consciousness during study period, change to sedatives, invasive monitoring)*	N=90 Age: 50.86 yrs. Female: 50% Ethnicity or Race: NR Marital status: NR	Medical ICU *days* MV: NR .	Mode: Not Reported Airway: ETT 100%

Key of abbreviations: AC: Assist Control, APACHE: Acute Physiology and Chronic Health Evaluation; CAM: BIS: Bispectral Index of Sedation; Confusion Assessment Method; CVICU: Cardiovascular ICU; GCS: ETT: Endotracheal tube; FiO2: Fractional inspired oxygen; Glasgow Coma Score, ICU: Intensive Care Unit; MV: Mechanical Ventilation, NR: not reported; PAV: Proportional Assist Ventilation; PCV: Pressure Control Ventilation; PEEP: Positive End Expiratory Pressure; PSV: pressure support ventilation; RASS: Richmond Agitation Sedation Scale; SAS: Sedation Agitation Scale; Trach: Tracheostomy tube

Table 2.4: **Music Intervention and Control Condition**

First Author, Publication Year	Music Intervention				Delivery of [Music] Intervention					Observation Interval
	Self-Select	Type/Style of music**	Tempo	Length of Intervention	Method of Delivery	Number of Interventions	Control Condition	Time of Day	Clinical Context	
Aktas, 2015	NO	Instrumental Reed Flute (Ney); Sufi composition (Huseyni & Nihavend modes)	60-80 rhythms/min no strong beat fluctuations	40 min (20 min before, during and 20 after procedure)	Ergonomic audio pillow, with MP3	Once	Usual care	Not Reported	Prior to during and after suctioning	Repeated measures: Baseline, 20 min, 40 min
Aktas, 2018	NO	Instrumental Reed Flute (Ney); Sufi composition(Huseyni & Nihavend modes)	60-80 rhythms/min no strong beats/ fluctuation	40 min (20 min before, during and 20 min after procedure)	Ergonomic audio pillow, with MP3	Once	Usual care	Not Reported	Prior to during and after suctioning	Repeated measures: Baseline, 20 min, 40 min
Almerud, 2002	NO	Western Classical (selection used in 3 previous, cited studies) **	Not Reported	30 min	Headphones	Once	Rest under similar conditions	Night bedtime	Lights dimmed; interruptions minimized	Repeated measures: baseline, 15 min, 30 min and 60 min
Beaulieu-Boire, 2013	NO	Western Classical: orchestral with strings **	Not Reported	60 min	Headphones	2x/day per group	Resting Quietly with Headphones	10:00 and 20:00	No major disruptions	Pre-test Posttest
Chlan, 1998	YES Limited Selection	Western Classical 56%, Country Western 28%, Easy Listening 12% New Age 4% Religious 0% All Non-lyric	60-80 beats/min	30 min	Headphones	Once	Resting Quietly	Not Reported	Closed blinds, dimmed lights, do not disturb (instructed to think pleasant thoughts, concentrate on music)	Pre-test Posttest

First Author, Publication Year	Music Intervention				Delivery of [Music] Intervention					Observation Interval
	Self-Select	Type/Style of music**	Tempo	Length of Intervention	Method of Delivery	Number of Interventions	Control Condition	Time of Day	Clinical Context	
Chlan, 2007	YES Limited Selection	All Non-lyric Western Classical100% Country Western 0% Easy Listening 0 New Age 0%	Not Reported	60 min	Headphones	Once	Resting Quietly	Early Morning: starting at 05:40	Not Reported	Repeated measures: baseline, T0+15", T0+30 min, T0+60 min
Chlan, 2013	YES Limited Selection	6 CD starter kit ('relaxing' piano, harp, guitar and Native American flute),	Not Reported	79.8 min/d	Headphones	minimum 2x/daily	Noise Cancelation headphones (34 min/day vs Usual care)	Not Reported	Instructed to use 'when feeling anxious'	Baseline then daily anxiety and sedative use throughout study period
Conrad, 2007	NO	Mozart, piano sonatas **	'slow movement'	60 min	Headphones	Once	Headphones	9:00	1st post-op day, 15 min after cessation of propofol	Pre-test, posttest
Damshens, 2018	NO	[mainly] instrumental music tracks	Not Reported	45 min	Not Reported	2x/day	Standard of Care	Morning and night	Not Reported	Summative comparison between groups
Dijkstra, 2010	YES Limited Selection	Western classical 5% or Easy Listening 95% (non-vocal) film scores **	'slow beats', 'relaxing'	30 min	Headphones with MP3 player	3 x over 2 days	Resting Quietly	10:00-12:00 and 20:00-22:00	12 subjects in shared room (Private: 6 control 2 intervention)disruptions minimized	Repeated measures Baseline, +5, +10 +20, +30 +60 min Pre-test, Posttest

First Author, Publication Year	Music Intervention				Delivery of [Music] Intervention					Observation Interval
	Self-Select	Type/Style of music**	Tempo	Length of Intervention	Method of Delivery	Number of Interventions	Control Condition	Time of Day	Clinical Context	
Han, 2010	YES Limited Selection	Western Classical 10% Western 'Light' 27% Chinese Traditional 47% Chinese Folk with lyrics 16%**	60-80 beats/ min, slow, flowing rhythms, all 'familiar to Chinese people'	30 min	Headphones with MP3 player	Once	Headphones without music vs Resting Quietly	Afternoon or early evening	Lights dimmed, do not disturb, blinds closed Instructed to lie quietly with eyes closed, think pleasant thoughts	Repeated measures (for physiologic variables) at 5 min intervals and 5 min post; pre-test/posttest for psychometrics
Iblher, 2011	NO	Baroque pieces played by organ, flute and string orchestra	60-80 beats/min	60 min	Headphones	Once	Headphones without music or usual care	Not Reported	Immediately post-operative, or immediately after sedation cessation	Pre-test posttest psychometric Total Rx consumption
Jaber, 2006	YES compiled by music therapist	6 pieces, 3-4 min each	Progressively more 'relaxing', seamless transition between pieces	20 min	Headphones	Once	Resting Quietly	10:00-20:00	Lying in bed, eyes closed, no IV medications for 2 hrs. prior, no physical therapy/ suctioning 1 hr. prior	Repeated Measures Baseline, T0+5min, +10 min, +20 min, pre-test/posttest for psychometrics
Jacq, 2018	NO	Mozart	Not Reported	During bed bath and for 30 min after	Headphones	Once	Usual care	8:00	During morning bed bathing	Psychometric tests: baseline, peak during bath, 30 min post bath, +60 min, + 120 min

First Author, Publication Year	Music Intervention				Delivery of [Music] Intervention					Observation Interval
	Self-Select	Type/Style of music**	Tempo	Length of Intervention	Method of Delivery	Number of Interventions	Control Condition	Time of Day	Clinical Context	
Khan, 2020	YES	Personalized not reported, Relaxing music arm 60-80 bpm piano, guitar, classical or Native American Flute**	Personalized not reported; investigator choices 60-80 beats per minute, 'relaxing'	60 min	Headphones	2x/day Up to 7d	Audio books and Investigator chosen music	9 am-11 am and 2pm-4pm	Not Reported	Twice daily delirium and pain, once daily anxiety
Korhan, 2011	NO	Western Classical** flute	60-66 beats/ min 'Relaxing'	60 min	Headphones	Once	NR	Not Reported	Propofol cessation 30 min prior	Repeated measures, baseline 30 min intervals during, 30 min post
Kyavar, 2016	YES Limited Selection	Quran 53%	Not Reported	30 min	Headphones	Once	Headphones no music	Not Reported	3-5 hrs. after operation, 'painful procedure' at end of 30 min study period	Pre-test-Posttest
Lee, 2017 **	YES Limited Selection	Western classical, Chinese classical, music of nature sounds, 'Relax you Mood', religious**	60-80 beats/min 'relaxing'	30 min	Headphones	Once	Noise cancellation headphones	16:00-16:30	Low lighting, room temperature 26, interruptions minimized	Repeated measures: vital signs, baseline and every 10 min, up to 30 min post Pre-test Posttest Psychometric and serum biomarkers

First Author, Publication Year	Music Intervention				Delivery of [Music] Intervention					Observation Interval
	Self-Select	Type/Style of music**	Tempo	Length of Intervention	Method of Delivery	Number of Interventions	Control Condition	Time of Day	Clinical Context	
Lee, 2005	YES Limited Selection	Chinese classical, religious, Western classical, music of nature sounds	'slow beats', 'relaxing'	30 min	Headphones	Once	Headphones no music	Not Reported	Lights and curtains closed, instructed to close eyes, single cubicle-room	Pre-test Post test
Liang, 2016	YES	Participant selection of genre, artist, instrument	60-80beats/min Instrumental only	60 min	Headphones	1x/day, 6 days	Not Reported	Not Reported	During daily ventilator weaning trial, interruptions minimized, lying quietly, eyes closed	Pre-test Post-test aggregated mean difference
Mateu-Capell, 2018	NO	New Age (Zen) music**	'relaxing properties', predictable/ harmonic melodies	60 min	Headphones	Once	Noise Cancellation headphones	Not Reported	Not Reported	Repeated Measures: 15 min interval physiological signs, hourly psychometric
Messika, 2019	YES	NR	NR	30 min	Headphones	Not Reported	Noise Cancellation HeadphonesUsual Care	Not Reported	Not Reported	Repeated Measures pre, post 30 min, 1, 2, up to 24 hours
Park, 2019	YES	Preferred: Korean Pop, Korean Oldies compared to Classical **	Classical choice: 'slow tempo and beat'	30 min	Headphones	Once each	No control (non - inferiority)	Not Reported	uninterrupted, lights and other stimulus minimized	Pretest, posttest
To, 2013	NO	Mozart Piano Sonatas	'slow' and 'relaxing'	4 hours	Headphones	Once	Headphones with no music	Morning during rounds	During morning sedation interruption	Pre-test posttest

First Author, Publication Year	Music Intervention				Delivery of [Music] Intervention					Observation Interval
	Self-Select	Type/Style of music**	Tempo	Length of Intervention	Method of Delivery	Number of Interventions	Control Condition	Time of Day	Clinical Context	
Twiss, 2006	YES Limited Selection	Commercial preparation** Films scores: 19; Piano improv 4; Mozart 5 Original scores 2	'relaxing'	Not Reported	Headphones	Once	Usual Care	During OR, post-op period	Standardized care environment for intra and post operation for cardiac surgery	Pre-test Posttest psychometric Single measures comparing means
Wong, 2001	YES Limited Selection	Chinese music (folk, Chinese or Western instruments) Buddhist, Western music (classical, film scores, piano)	'relaxing'	30 min	Headphones	Once each	Resting Quietly	'non busy' visiting hours	Do not disturb, lights dimmed, curtains drawn/door closed, instructed to close eyes and concentrate on music/rest	Repeated measures physiological signs, 5 min Pre-test Posttest psychometric test
Yaghoubinia, 2016	NO	Instrumental music**	Not sad or exciting, with smooth rhythm and melody	30 min	Headphones	1x/day 3days	Reflexology vs Usual Care	16:00-18:00 'non busy time'	Not Reported	Pre-test posttest

** Specific music selections where noted: **Almerud**, **et. al**: Beethoven 'Suite 1 from Sonata in C-sharp minor (Moonlight Sonata)', Pachebel 'Canon', Debussy 'Calire de Lune', Bach 'Air from Suite for Orchestra no 3.', Vivaldi 'Spring: Largo', Seymer Sologa [Suneye], Marcello 'Concerto for oboe in D minor: Adagio; **Bealieu-Boire, et. al**: Bach (Air from Suite, Orchestra No3), Bach (Air for G string), Beethoven (Moonlight Sonata), Beethoven (Pathetic Sonata), Brahms (Lullaby), Chopin (Nocturne in G), Debussy (Claire de Lune) Pachelbel (Cannon in D), St-Saens (The Swan), Tchaikovsky (Panorama from Sleeping Beauty); **Conrad et. al**: "Andante", "Andantino con espressione", "Andante cantabile", "Adagio", "Andante cantabile", " Andante", "Adagio" and "Adagio"; **Dijkstra, et al**: Anton Bruckner: Quintet F-Dur, Adagio and Gustav Mahler: Symphony No 4 G-Dur, Ruhevoll, or Vangelis 1492 film score; **Han, et. al**: Western Classical – "Moonlight Sonata", "Appassionata", Western Light- "Brahms Lullaby", "Ballade pour Adeline", Chinese traditional- "Butterfly Lovers", "Moonlight of Spring River", Chinese Folk- "Song of Jasmine", "Rhythm of a Running Stream"; **Kahn, et al** Lifescapes Relaxing Piane, John Story or Watermark, Enya; **Korhan,**

Korshid, & Uyar: Bach's 19 trio sonatas played by James Galway; **Lee, et al**: Erik Satie Trios Gymnopedies, Mozart Piano Concerto No 26, Chinese classical bamboo flute, rain and tears, 'Sylvan Spa', 'Relax Your Mood'- 8 songs of nature sounds; **Mateu-Capell, et al**: Andreas Mock Reiki, the Light Touch from Merlin's Magic; **Park & Park**: Preferred: "Some", "Travel" and "Galaxy" by BOL4, "Let it Rain", " Drifting Apart" and "Loop" by NELL, "you Raise me Up" by Josh Groban, and "A woman out of a window" and "Bounce", Mona Lisa" and "The dreams" by Jo Yong-Pil, Classical Arm: Meditation: Classical Relaxation vol 3: Adagio, Romanze in F-Moll op 11, Peer Gynt Suite No.2, Op.55:IV Solveig's Song, Romane No. 2 for Violin, Ballet Music in G, From 'Rosamun, Symphony No.5 Adagietto'; **To et. al**: Mozart Piano Sonata Playlist all performed by Andras Schiff, Piano Sonata No 5 in G Andante, No 9 in D Andantino con espressione, No 10 in C major, Andante cantabile, No 12 in F Adagio, No 13 in B flat Andante cantabile, No 16 in C Sonata facile, No 17 in B flat, Adagio, No 18 in D Adagio; **Twiss, et al**: Prescriptive Music Inc, Clarity, Timeless, Towards, Interlude; **Yaghoubina, et al**: Arnd Stein (Strandspaziergang Beach Walk, from the album Top Hits zum Enst

Table 2.5: Outcomes Measured

First Author Year	Physiologic Measurements							Psychometric Measurements**						Vent Wean **	Self-Report Instruments					Serum Bio markers	Rx
	HR	SBP	DBP	MAP	RR	O2 sat	EEG BIS	CPOT	BPS	RASS	Ramsay	Sedic	CAM		NRS	VASA	VASD	STAI	PDI		
Aktas 2015	–	–	–			–		↓			↑										
Aktas 2018								↓	↓												
Almerud 2002	–	↓	↓		–	–															
Beaulieu-Boire 2013	–	–			–															↓ **cortisol** **↑ACTH** – Leptin	–
Chlan, 1998	↓				↓													↓			
Chlan, 2007	–																			– Epi cortisol, NE	
Chlan, 2013																↓				↓	–*
Conrad, 2007	–	↓					–				↑									**↓IL-6** **↓Epi** **↑GH** – Prolactin ACTH NE	

First Author Year	Physiologic Measurements							Psychometric Measurements**						Vent Wean **	Self-Report Instruments					Serum Bio markers	Rx
	HR	SBP	DBP	MAP	RR	O2 sat	EEG BIS	CPOT	BPS	RASS	Ramsay	Sedic	CAM		NRS	VAS A	VAS D	STAI	PDI		
Damshens, 2018													–								–
Dijkstra, 2010	–	–	–	–	–						↑ 1st session	–									
Han, 2010	↓	↓	↓		↓	–												↓			
Iblher, 2011	–	–	–			–									↑				–		–
Jaber, 2006	↓	↓	–	–	↓		↓			↓					↓						
Jacq, 2018	–	–	–	–	–				↓												
Khan, 2020										–			–			–					–
Korhan, 2011	–	↓	↓		↓	–															
Kyavar, 2016									↓												
Lee, 2005	↓	–	–		↓													–			
Lee, 2017 **	↓	↓	–	(↓)		–										↓		↓		↓ cortisol	
Liang, 2016	↓				↓									↑		–	↓				
Mateu-Capell, 2018	–	–	–		–		–		–		–										

First Author Year	Physiologic Measurements							Psychometric Measurements**						Vent Wean **	Self-Report Instruments					Serum Bio markers	Rx
	HR	SBP	DBP	MAP	RR	O2 sat	EEG BIS	CPOT	BPS	RASS	Ramsay	Sedic	CAM		NRS	VAS A	VAS D	STAI	PDI		
Messika, 2019																	–		↓		
Park, 2019										↓						↓		↓			
To, 2013											–			↑							↓
Twiss, 2006																		↓			
Wong, 2001				–	–													↓			
Yaghoubinia 2016							=		↓												

Key: Vent wean: Tolerance to ventilator weaning; HR = Mean Heart Rate measured in beats/min, SBP= Mean Systolic Blood Pressure measured in mmHg, DBP = Mean Diastolic Blood Pressure measured in mmHg, MAP = Mean Arterial Blood Pressure measured in mmHg, RR = Mean Respiratory Rate measured in breaths/min, O2sat = mean oxygen saturation, EEG= electroencephalogram changes consistent with relaxation (occipital, temporal, frontal leads), CPOT = Critical Care Pain Observation Tool, BPS= Behavior Pain Scale; RASS = Richmond Agitation Sedation Score (-5 to +4), Ramsay = Ramsay Scale; Sedic = Sedic Scale (Agitation/Sedation), CAM = Confusion Assessment Method, NRS= Numerical Rating Scale (Pain) (1-10), VAS-A= Visual Analogue Scale Anxiety (1-100), VAS-D= Visual Analogue Scale for Dyspnea (1-100); STAI= [Spielberg] State-Trait Anxiety Inventory; Patient Distress Index = PDI; Rx = Medication use; ACTH= acetylcholine; NE = norepinephrine **↓= statistically significant reduction, ↑= statistically significant increase,** – = outcome measured, but result not statistically significant.

Appendix 2.1: **Search Terms**

Patients	Settings	Intervention	Outcomes (Symptoms)
'respiration artificial' 'mechanical ventilation’	‘critical care’ ‘intensive care units’ ‘post-operative care’	'music' 'music medicine' 'music therapy' ‘music intervention’	‘pain’ 'anxiety’ 'agitation’ ‘sedation’ ‘sedative’ ‘delirium’ ‘confusion’ ‘disorientation’ ‘stress’ ‘sleep’ ‘insomnia’ ‘fear’ ‘satisfaction’ ‘loneliness’ ‘depression’ ‘dyspnea’ ‘shortness of breath’

Appendix 2.2: **Qualitative Findings**

Almerud, 2002: No recall of listening to music; 'constant light and noise' a source of discomfort, confusion; comfort from family presence

Chlan, 2013: sleeping while listening, tapping along, appears less anxious to nursing, 'rests well' with the headphones, seems happy, slept well with music on, calm resting; able to decrease sedative

Conrad, 2007: No extra sedative in RMLI arm, rescue sedative in control condition

Khan, 2020: music made them feel 'normal and calm', 80% rated music enjoyable, would prefer to choose their own

Lee, 2005: increase in proportion of 'comfort behaviors, such as ‘restfulness’ and ‘sleep’

Mateu-Capell, 2018: observed waking from sedation, fell asleep if music on

Park, 2019: change in agitated behaviors stopped once preferred music on (e.g., no longer trying to take off a medical device); smiling moving lips to sing along, disappointed only allowed to listen to preferred music once, fun to listen to preferred

References

1. SCCM. http://www.sccm.org/Communications/Pages/CriticalCareStats.aspx 2018 [
2. Adhikari NK, Fowler RA, Bhagwanjee S, Rubenfeld GD. Critical care and the global burden of critical illness in adults. Lancet (London, England). 2010;376(9749):1339-46.
3. Granberg A, Bergbom Engberg I, Lundberg D. Patients' experience of being critically ill or severely injured and cared for in an intensive care unit in relation to the ICU syndrome. Part I. Intensive & critical care nursing. 1998;14(6):294-307.
4. Rotondi AJ, Chelluri L, Sirio C, Mendelsohn A, Schulz R, Belle S, et al. Patients' recollections of stressful experiences while receiving prolonged mechanical ventilation in an intensive care unit. Critical care medicine. 2002;30(4):746-52.
5. Lewandowska K, Mędrzycka-Dąbrowska W, Pilch D, Wach K, Fortunato A, Krupa S, et al. Sleep Deprivation from the Perspective of a Patient Hospitalized in the Intensive Care Unit-Qualitative Study. Healthcare (Basel). 2020;8(3):351.
6. Topcu S, Alpar S, Karabacak B, Kebapcı A. Patient experiences in intensive care units: a systematic review. Patient Experience Journal. 2017;4:115-27.
7. Von Rueden KT, Wallizer B, Thurman P, McQuillan K, Andrews T, Merenda J, et al. Delirium in Trauma Patients: Prevalence and Predictors. Crit Care Nurse. 2017;37(1):40-8.
8. Zaal IJ, Devlin JW, Peelen LM, Slooter AJ. A systematic review of risk factors for delirium in the ICU. Critical care medicine. 2015;43(1):40-7.
9. Li DT, Puntillo K. A pilot study on coexisting symptoms in intensive care patients. Applied nursing research : ANR. 2006;19(4):216-9.

10. Puntillo K, Arai S, Cohen N, Gropper M, Neuhaus J, Paul S, et al. Symptoms experienced by intensive care unit patients at high risk of dying. Critical care medicine. 2010;38(11):2155-60.

11. Puntillo K, Nelson JE, Weissman D, Curtis R, Weiss S, Frontera J, et al. Palliative care in the ICU: relief of pain, dyspnea, and thirst--a report from the IPAL-ICU Advisory Board. Intensive care medicine. 2014;40(2):235-48.

12. Ahmad IM, editor Relationship between anxiety and fear levels and the weaning success or failure of mechanically ventilated patients2018.

13. Barr J, Fraser GL, Puntillo K, Ely EW, Gelinas C, Dasta JF, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Critical care medicine. 2013;41(1):263-306.

14. Tate JA. Anxiety and Agitation in Mechanically Ventilated Patients. 2012;22(2):157-73.

15. Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Critical care medicine. 2001;29(7):1370-9.

16. Lat I, McMillian W, Taylor S, Janzen JM, Papadopoulos S, Korth L, et al. The impact of delirium on clinical outcomes in mechanically ventilated surgical and trauma patients. Critical care medicine. 2009;37(6):1898-905.

17. Pandharipande P, Cotton BA, Shintani A, Thompson J, Pun BT, Morris JA, Jr., et al. Prevalence and risk factors for development of delirium in surgical and trauma intensive care unit patients. The Journal of trauma. 2008;65(1):34-41.

18. Burry LD, Williamson DR, Mehta S, Perreault MM, Mantas I, Mallick R, et al. Delirium and exposure to psychoactive medications in critically ill adults: A multi-centre observational study. Journal of critical care. 2017;42:268-74.

19. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. Anesthesiology. 2006;104(1):21-6.

20. Ouimet S, Kavanagh BP, Gottfried SB, Skrobik Y. Incidence, risk factors and consequences of ICU delirium. Intensive care medicine. 2007;33(1):66-73.

21. Johnson P, St John W, Moyle W. Long-term mechanical ventilation in a critical care unit: existing in an uneveryday world. Journal of advanced nursing. 2006;53(5):551-8.

22. Nikayin S, Rabiee A, Hashem MD, Huang M, Bienvenu OJ, Turnbull AE, et al. Anxiety Symptoms in Survivors of Critical Illness: A Systematic Review and Meta-Analysis. General hospital psychiatry. 2016;43:23-9.

23. Lof L, Berggren L, Ahlstrom G. ICU patients' recall of emotional reactions in the trajectory from falling critically ill to hospital discharge: follow-ups after 3 and 12 months. Intensive & critical care nursing. 2008;24(2):108-21.

24. Tanaka LMS, Azevedo LCP, Park M, Schettino G, Nassar AP, Réa-Neto A, et al. Early sedation and clinical outcomes of mechanically ventilated patients: a prospective multicenter cohort study. Critical Care. 2014;18(4):R156.

25. Litton E, Carnegie V, Elliott R, Webb SA. The Efficacy of Earplugs as a Sleep Hygiene Strategy for Reducing Delirium in the ICU: A Systematic Review and Meta-Analysis. Critical care medicine. 2016;44(5):992-9.

26. McGrane S, Pandharipande PP. Sedation in the intensive care unit. Minerva anestesiologica. 2012;78(3):369-80.

27. Samuelson KA, Lundberg D, Fridlund B. Stressful experiences in relation to depth of sedation in mechanically ventilated patients. Nursing in critical care. 2007;12(2):93-104.

28. Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJC, Pandharipande PP, et al. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Critical care medicine. 2018;46(9):e825-e73.

29. Gouk P. An Enlightenment proposal for music therapy: Richard Brocklesby on music, spirit, and the passions. Progress in brain research. 2015;217:159-85.

30. Nightingale F. Notes on Nursing. What It Is, And What It Is Not. Edinborough: Churchil Livingstone; 1859/1980.

31. A model for symptom management. The University of California, San Francisco School of Nursing Symptom Management Faculty Group. Image--the journal of nursing scholarship. 1994;26(4):272-6.

32. Robb SL, Hanson-Abromeit D, May L, Hernandez-Ruiz E, Allison M, Beloat A, et al. Reporting quality of music intervention research in healthcare: A systematic review. Complementary therapies in medicine. 2018;38:24-41.

33. Tracy MF, Chlan L. Nonpharmacological interventions to manage common symptoms in patients receiving mechanical ventilation. Crit Care Nurse. 2011;31(3):19-28.

34. Meghani N, Tracy MF, Hadidi NN, Lindquist R. Part I: The Effects of Music for the Symptom Management of Anxiety, Pain, and Insomnia in Critically Ill Patients: An Integrative Review of Current Literature. Dimens Crit Care Nurs. 2017;36(4):234-43.

35. Stegemann T, Geretsegger M, Phan Quoc E, Riedl H, Smetana M. Music Therapy and Other Music-Based Interventions in Pediatric Health Care: An Overview. Medicines (Basel, Switzerland). 2019;6(1):25.

36. Tracy MF, Lindquist R, Savik K, Watanuki S, Sendelbach S, Kreitzer MJ, et al. Use of complementary and alternative therapies: a national survey of critical care nurses. Am J Crit Care. 2005;14(5):404-14; quiz 15-16.

37. Cooke M, Mitchell M, Tiralongo E, Murfield J. Complementary and alternative medicine and critical care nurses: a survey of knowledge and practices in Australia. Aust Crit Care. 2012;25(4):213-23.

38. Cutshall S, Derscheid D, Miers AG, Ruegg S, Schroeder BJ, Tucker S, et al. Knowledge, attitudes, and use of complementary and alternative therapies among clinical nurse specialists in an academic medical center. Clin Nurse Spec. 2010;24(3):125-31.

39. Richard-Lalonde M, Gélinas C, Boitor M, Gosselin E, Feeley N, Cossette S, et al. The Effect of Music on Pain in the Adult Intensive Care Unit: A Systematic Review of Randomized Controlled Trials. Journal of Pain and Symptom Management. 2020;59(6):1304-19.e6.

40. Umbrello M, Sorrenti T, Mistraletti G, Formenti P, Chiumello D, Terzoni S. Music therapy reduces stress and anxiety in critically ill patients: a systematic review of randomized clinical trials. Minerva anestesiologica. 2019.

41. Garcia Guerra G, Almeida L, Zorzela L, King-Jones S, Joffe AR, Hartling L, et al. Efficacy of music on sedation, analgesia and delirium in critically ill patients. A systematic review of randomized controlled trials. Journal of critical care. 2019;53:75-80.

42. Bradt J, Dileo C. Music interventions for mechanically ventilated patients. The Cochrane database of systematic reviews. 2014(12):Cd006902.

43. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of clinical epidemiology. 2009;62(10):e1-34.

44. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Journal of clinical epidemiology. 2009;62(10):1006-12.

45. Robb SL, Burns DS, Carpenter JS. Reporting guidelines for music-based interventions. J Health Psychol. 2011;16(2):342-52.

46. Kennedy CE, Fonner VA, Armstrong KA, Denison JA, Yeh PT, O'Reilly KR, et al. The Evidence Project risk of bias tool: assessing study rigor for both randomized and non-randomized intervention studies. Systematic Reviews. 2019;8(1):3.

47. Lee CH, Lai CL, Sung YH, Lai MY, Lin CY, Lin LY. Comparing effects between music intervention and aromatherapy on anxiety of patients undergoing mechanical ventilation in the intensive care unit: a randomized controlled trial. Quality of Life Research. 2017;26(7):1819-29.

48. Lee CH, Lee CY, Hsu MY, Lai CL, Sung YH, Lin CY, et al. Effects of Music Intervention on State Anxiety and Physiological Indices in Patients Undergoing Mechanical Ventilation in the Intensive Care Unit: A Randomized Controlled Trial. Biological Research for Nursing. 2017;19(2):137-44.

49. Mateu-Capell M, Arnau A, Juvinyà D, Montesinos J, Fernandez R. Sound isolation and music on the comfort of mechanically ventilated critical patients. Nursing in critical care. 2019;24(5):290-8.

50. Twiss E, Seaver J, McCaffrey R. The effect of music listening on older adults undergoing cardiovascular surgery. Nursing in critical care. 2006;11(5):224-31.

51. Almerud S, Petersson K. Music therapy--a complementary treatment for mechanically ventilated intensive care patients. Intensive & critical care nursing. 2003;19(1):21-30.

52. Jong Yoen P, Soohyun P. Effects of Two Music Therapy Methods on Agitation and Anxiety among Patients Weaning off Mechanical Ventilation: A Pilot Study. Journal of Korean Academy of Fundamentals of Nursing. 2019;26(2):136-43.

53. Han L, Li JP, Sit JW, Chung L, Jiao ZY, Ma WG. Effects of music intervention on physiological stress response and anxiety level of mechanically ventilated patients in China: a randomised controlled trial. J Clin Nurs. 2010;19(7-8):978-87.

54. Korhan EA, Khorshid L, Uyar M. The effect of music therapy on physiological signs of anxiety in patients receiving mechanical ventilatory support. Journal of Clinical Nursing. 2011;20(7-8):1026-34.

55. Chlan L. Effectiveness of a music therapy intervention on relaxation and anxiety for patients receiving ventilatory assistance. Heart & lung : the journal of critical care. 1998;27(3):169-76.

56. Lee OKA, Chung YFL, Chan MF, Chan WM. Music and its effect on the physiological responses and anxiety levels of patients receiving mechanical ventilation: A pilot study. Journal of Clinical Nursing. 2005;14(5):609-20.

57. Damshens MH, Sanie MS, Javadpour S, Khaef MA, Rastgarian A. The Role of Music on the Delirium in Traumatic Patients: A Case Study in the ICU of Peymanieh Hospital of Jahrom, Fars Province, Iran. Ambient Science. 2018;5:97-101.

58. Beaulieu-Boire G, Bourque S, Chagnon F, Chouinard L, Gallo-Payet N, Lesur O. Music and biological stress dampening in mechanically-ventilated patients at the intensive care unit ward-a prospective interventional randomized crossover trial. Journal of critical care. 2013;28(4):442-50.

59. Chlan L, Engeland W, Anthony A, Guttormson J. Influence of music on the stress response in patients receiving mechanical ventilatory support: a pilot study. Am J Crit Care. 2007;16(2):141-5.

60. Conrad C, Niess H, Jauch KW, Bruns CJ, Hartl WH, Welker L. Overture for growth hormone: Requiem for interleukin-6? Critical care medicine. 2007;35(12):2709-13.

61. Iblher P, Mahler H, Heinze H, Hüppe M, Klotz KF, Eichler W. Does music harm patients after cardiac surgery? A randomized, controlled study. Applied Cardiopulmonary Pathophysiology. 2011;15(1):14-23.

62. Jacq G, Melot K, Bezou M, Foucault L, Courau-Courtois J, Cavelot S, et al. Music for pain relief during bed bathing of mechanically ventilated patients: A pilot study. PloS one. 2018;13(11):e0207174-e.

63. Liang Z, Ren DX, Choi JY, Happ MB, Hravnak M, Hoffman LA. Music intervention during daily weaning trials-A 6 day prospective randomized crossover trial. Complementary therapies in medicine. 2016;29:72-7.

64. Wong HLC, Lopez-Nahas V, Molassiotis A. Effects of music therapy on anxiety in ventilator-dependent patients. Heart and Lung: Journal of Acute and Critical Care. 2001;30(5):376-87.

65. Aktas Y, Karabulut N. The effects of music therapy in endotracheal suctioning of mechanically ventilated patients. Nursing in critical care. 2016;21(1):44-52.

66. Jaber S, Bahloul H, Guétin S, Chanques G, Sebbane M, Eledjam JJ. Effects of music therapy in intensive care unit without sedation in weaning patients versus non-ventilated patients. Annales Francaises d'Anesthesie et de Reanimation. 2007;26(1):30-8.

67. Aktas Y, Karabulut N. Relief of Procedural Pain in Critically Ill Patients by Music Therapy: A Randomized Controlled Trial. Complementary medicine research. 2019:1-9.

68. Dijkstra BM, Gamel C, van der Bijl JJ, Bots ML, Kesecioglu J. The effects of music on physiological responses and sedation scores in sedated, mechanically ventilated patients. Journal of clinical nursing. 2010;19(7-8):1030-9.

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

70. Yaghoubinia F, Navidian A, Sheikh S, Safarzai E, Tabatabaei S. Effect of music therapy and reflexology on pain in unconscious patients: A randomized clinical trial. International Journal of Medical Research & Health Sciences. 2016;5(9):288-95.

71. Kyavar M, Karkhaneh S, Rohanifar R, Azarfarin R, Sadeghpour A, Alizadehasl A, et al. Effect of preferred music listening on pain reduction in mechanically ventilated patients after coronary artery bypass graft surgery. Research in Cardiovascular Medicine. 2016;5(4).

72. Chlan L, Weinert C, Heiderscheit A, Tracy M, Skaar D, Guttormson J, et al. Effects of patient-directed music intervention on anxiety and sedative exposure in critically ill patients receiving mechanical ventilatory support: a randomized clinical trial. Jama. 2013;309(22):2335-44.

73. Khan SH, Xu CJ, Purpura R, Durrani S, Lindroth H, Wang S, et al. DECREASING DELIRIUM THROUGH MUSIC: A RANDOMIZED PILOT TRIAL. American Journal of Critical Care. 2020;29(2):E31-E8.

74. To WTH, Bertolo T, Dinh VA, Jichici D, Hamielec CM. Mozart Piano Sonatas as a Nonpharmacological Adjunct to Facilitate Sedation Vacation in Critically Ill Patients. Music and medicine. 2013;5:119-27.

75. Grap M, Munro C, Wetzel P, Best A, Ketchum J, Hamilton V, et al. Sedation in adults receiving mechanical ventilation: physiological and comfort outcomes. Am J Crit Care. 2012;21(3):e53-63; quiz e4.

76. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med. 2002;166(10):1338-44.

77. Ely EW, Truman B, Shintani A, Thomason JW, Wheeler AP, Gordon S, et al. Monitoring sedation status over time in ICU patients: reliability and validity of the Richmond Agitation-Sedation Scale (RASS). Jama. 2003;289(22):2983-91.

78. Murrock CJ, Bekhet AK. Concept Analysis: Music Therapy. Research and theory for nursing practice. 2016;30(1):44-59.

79. Koelsch S, Jancke L. Music and the heart. European heart journal. 2015;36(44):3043-9.

80. Yackle K, Schwarz LA, Kam K, Sorokin JM, Huguenard JR, Feldman JL, et al. Breathing control center neurons that promote arousal in mice. Science (New York, NY). 2017;355(6332):1411-5.

81. Thoma MV, La Marca R, Bronnimann R, Finkel L, Ehlert U, Nater UM. The effect of music on the human stress response. PloS one. 2013;8(8):e70156.

82. Peeters B, Langouche L, Van den Berghe G. Adrenocortical Stress Response during the Course of Critical Illness. Comprehensive Physiology. 2017;8(1):283-98.

83. Vanhorebeek I, Van den Berghe G. The neuroendocrine response to critical illness is a dynamic process. Critical care clinics. 2006;22(1):1-15, v.

84. Boonen E, Vervenne H, Meersseman P, Andrew R, Mortier L, Declercq PE, et al. Reduced cortisol metabolism during critical illness. The New England journal of medicine. 2013;368(16):1477-88.

85. Williamson PR, Altman DG, Bagley H, Barnes KL, Blazeby JM, Brookes ST, et al. The COMET Handbook: version 1.0. Trials. 2017;18(3):280.

86. Jespersen KV, Koenig J, Jennum P, Vuust P. Music for insomnia in adults. The Cochrane database of systematic reviews. 2015(8):Cd010459.

87. Su CP, Lai HL, Chang ET, Yiin LM, Perng SJ, Chen PW. A randomized controlled trial of the effects of listening to non-commercial music on quality of nocturnal sleep and relaxation indices in patients in medical intensive care unit. Journal of advanced nursing. 2013;69(6):1377-89.

88. Hu RF, Jiang XY, Hegadoren KM, Zhang YH. Effects of earplugs and eye masks combined with relaxing music on sleep, melatonin and cortisol levels in ICU patients: a randomized controlled trial. Critical care (London, England). 2015;19:115.

89. Ploghaus A, Narain C, Beckmann CF, Clare S, Bantick S, Wise R, et al. Exacerbation of Pain by Anxiety Is Associated with Activity in a Hippocampal Network. The Journal of Neuroscience. 2001;21(24):9896.

90. Gross RT, Collins FL. On the relationship between anxiety and pain: A methodological confounding. Clinical Psychology Review. 1981;1(3):375-86.

91. Aghdaii N, Yazdanian F, Faritus SZ. Sedative efficacy of propofol in patients intubated/ventilated after coronary artery bypass graft surgery. Anesthesiology and pain medicine. 2014;4(1):e17109.

92. La G, Gerdner L. Evidence-Based Guideline: Individualized Music in Persons with Dementia (6th Edition). 2019.

93. Cardozo M. Harmonic sounds: complementary medicine for the critically ill. Br J Nurs. 2004;13(22):1321-4.

94. White JM. State of the science of music interventions. Critical care and perioperative practice. Crit Care Nurs Clin North Am. 2000;12(2):219-25.

95. Allen K, Golden LH, Izzo JL, Jr., Ching MI, Forrest A, Niles CR, et al. Normalization of hypertensive responses during ambulatory surgical stress by perioperative music. Psychosomatic medicine. 2001;63(3):487-92.

96. Heiderscheit A, Chlan L, Donley K. Instituting a music listening intervention for critically ill patients receiving mechanical ventilation: Exemplars from two patient cases. Music and medicine. 2011;3(4):239-46.

97. Fontaine DK. Nonpharmacologic management of patient distress during mechanical ventilation. Critical care clinics. 1994;10(4):695-708.

98. Heiderscheit A, Breckenridge SJ, Chlan LL, Savik K. Music preferences of mechanically ventilated patients participating in a randomized controlled trial. Music and medicine. 2014;6(2):29-38.

99. Park S, Williams RA, Lee D. Effect of Preferred Music on Agitation After Traumatic Brain Injury. Western journal of nursing research. 2016;38(4):394-410.

100. Heine L, Tillmann B, Hauet M, Juliat A, Dubois A, Laureys S, et al. Effects of preference and sensory modality on behavioural reaction in patients with disorders of consciousness. Brain injury. 2017;31(10):1307-11.

101. MacClelland DC. Music in the operating room. AORN journal. 1979;29(2):252-60.

102. Salamon E, Bernstein SR, Kim SA, Kim M, Stefano GB. The effects of auditory perception and musical preference on anxiety in naive human subjects. Medical science monitor : international medical journal of experimental and clinical research. 2003;9(9):Cr396-9.

103. van den Bosch I, Salimpoor VN, Zatorre RJ. Familiarity mediates the relationship between emotional arousal and pleasure during music listening. Frontiers in Human Neuroscience. 2013;7:534.

104. Farnsworth P. The Social Psychology of Music. 2nd ed. Ames, Iowa: The Iowa State University Press 1969. 298 p.

105. Puntillo KA, Neuhaus J, Arai S, Paul SM, Gropper MA, Cohen NH, et al. Challenge of assessing symptoms in seriously ill intensive care unit patients: can proxy reporters help? Critical care medicine. 2012;40(10):2760-7.

106. Brach C, Fraser I. Can cultural competency reduce racial and ethnic health disparities? A review and conceptual model. Medical care research and review : MCRR. 2000;57 Suppl 1:181-217.

107. Darbyshire JL, Young JD. An investigation of sound levels on intensive care units with reference to the WHO guidelines. Critical care (London, England). 2013;17(5):R187.

108. Tainter CR, Levine AR, Quraishi SA, Butterly AD, Stahl DL, Eikermann M, et al. Noise Levels in Surgical ICUs Are Consistently Above Recommended Standards. Critical care medicine. 2016;44(1):147-52.

109. Gallacher S, Enki D, Stevens S, Bennett MJ. An experimental model to measure the ability of headphones with active noise control to reduce patient's exposure to noise in an intensive care unit. Intensive Care Med Exp. 2017;5(1):47.

110. Castro M, Tillmann B, Luauté J, Corneyllie A, Dailler F, André-Obadia N, et al. Boosting Cognition with Music in Patients with Disorders of Consciousness. Neurorehabilitation and neural repair. 2015;29(8):734-42.

111. Edlow BL, Chatelle C, Spencer CA, Chu CJ, Bodien YG, O'Connor KL, et al. Early detection of consciousness in patients with acute severe traumatic brain injury. Brain. 2017;140:2399-414.

112. Rahimi F, Saleh, K., Seidi, J. The effect of pleasant audio stimulation on the level of consciousness of comatose patient: a randomized clinical trial. Acta Medica Meditterranea 2019;35:985-9.

113. Sun J, Chen W. Music therapy for coma patients: preliminary results. European review for medical and pharmacological sciences. 2015;19(7):1209-18.

114. Girard TD, Kress JP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. Lancet (London, England). 2008;371(9607):126-34.

115. Kahloul M, Mhamdi S, Nakhli MS, Sfeyhi AN, Azzaza M, Chaouch A, et al. Effects of music therapy under general anesthesia in patients undergoing abdominal surgery. The Libyan journal of medicine. 2017;12(1):1260886.

116. Chlan L, Savik K. Patterns of anxiety in critically ill patients receiving mechanical ventilatory support. Nursing research. 2011;60(3 Suppl):S50-S7.

117. Joober R, Schmitz N, Annable L, Boksa P. Publication bias: What are the challenges and can they be overcome? Journal of Psychiatry & Neuroscience : JPN. 2012;37(3):149-52.

Chapter 3: Personally Selected Recorded Music for Cognitive and Psychological Homeostasis in Critical Care

Abstract

Purpose: Mechanically ventilated adults experience significant symptom burden during critical care hospitalization. Pain, anxiety, and delirium and the medications used to treat each are associated with increased morbidity and long-term negative cognitive and psychological outcomes. Recorded music has been used as an adjunct for symptom management in critical care but remains understudied in terms of population diversity, music selection, and range of symptom experience. This study aims to illuminate the ways in which a diverse group of adults use self-selected recorded music to recover after critical illness and describe patients' perceptions of the effects of listening to self-selected music on symptom experience during MV after critical injury.

Methods: Semi-structured interviews were collected and analyzed with grounded theory methodology.

Setting: Surgical and Neurotrauma Intensive Care Unit (ICU) in an urban, level 1, academic hospital.

Participants: 16 critical informants (patients or their family) experiencing ICU hospitalization after critical injury.

Results: We identified 6 novel uses of personally selected music in ICU: 1) Restoring consciousness; 2) Maintaining cognition; 3) Humanizing the hospital experience; 4) Providing source of connection; 5) Improving psychological wellbeing; and 6) Resolving the problems of silence. Few participants described the use of recorded music for pain or anxiety. People used recorded music to access music related memories and address complex psychological

experiences of loneliness, fear, de-situation, confusion, threats to identity and loss of control. Listening to self-selected music helped people regain their sense of self, their humanity, and to begin to process their trauma and grief. Additional benefits of listening to recorded music included experiencing joy, pleasure, hope, resilience, and feelings of normalcy. Participants identified an aversion to being sedated, preferring to be awake and aware, and music helped them to achieve this state. This study also highlighted the problems people experienced with silence and a lack of meaningful stimulation in critical care.

Conclusion: Critically injured adults used music to achieve psychological and cognitive homeostasis during their ICU hospitalization. These results are encouraging for future studies designed to explore the use of recorded music to prevent and treat the cognitive and emotional morbidity of ICU hospitalization.

Key Words: Music, Critical Care, Symptoms, Cognition, Delirium, Humanism, Loneliness, Consciousness

Introduction

Over 4 million adults are admitted annually to intensive care units (ICU) in the United States (US) (1). Advanced respiratory support with mechanical ventilation (MV) is the most common intervention used in critical care (2). In the US between 20-40% of adults receive MV during their ICU admission, and global estimates are between 13- 20 million people per year (1,2). Critically ill and injured adults experience significant symptom burden, reporting high rates of pain, anxiety, restlessness, dyspnea, confusion, and sleep disorders (3-6). MV is an independent risk factor for each of these distressing symptoms (7, 8). Medications used to manage symptoms in ICU are of limited effectiveness and several are associated with significant side effects including an increased risk of delirium (9-11). Delirium causes significant physical and emotional distress and may affect recovery, resulting in increased length of MV, longer ICU stays and cognitive impairment (10, 12-16). Patients in critical care also endorse a series of troubling psychological symptoms not amenable to pharmacologic interventions, including extreme loneliness, feelings of dependence, lack of communication, fear and de-situatedness (6, 17-19). Undermanaged psychological symptoms and delirium are, in turn, associated with the development of long-term psychological and cognitive symptoms including anxiety, depression, post-traumatic stress, cognitive impairment, functional disability, and decreased quality of life referred to as post-intensive care syndrome (PICS) (20, 21). Heightened awareness of the risk of medication side effects, coupled with the imperative to manage distressing symptoms and improve patient outcomes, has led to increased interest in nonpharmacologic interventions, such as music, for symptom management in critical care.

Music is the making, invoking, or listening to the arrangement of sound over time, through the elements of pitch, rhythm, tempo, contour, timbre, loudness, meter, harmony

(consonance), and melody (22). Seashore, a pioneer of psychology of music, examined the cognitive, processing, affective nature of, and response to music through a series of controlled experiments focused on the perception of these elements (23). Missing from Seashore's studies, however, was consideration of factors such as an individual's social context, cultural values, prior experiences, and music preference. The influence of these factors was later described in Farnsworth's treatise *The Social Psychology of Music* (24). In this work, Farnsworth concludes that it is personal music preference and degree of familiarity that determine our psychophysiological responses music. These views are echoed in the writings of Damasio and Zatorre who, through empiric studies, have shown a relationship between preference, familiarity, and the psychobiological effects of listening to music, and who have developed theoretical frameworks to describe the complex social and cognitive neuroscientific phenomenon of music (25-28).

Listening to music has long been reported to have psychological benefits appearing in ancient texts as a 'salve' and a pathway to improved ability, wellness and strength (29). Well before the advent of the modern ICU, ancient Greeks healed anxious patients with musical instruments, they quieted their minds and lulled them to sleep using a lyre, opining that through music one could attain a harmony of body and soul (30). In the mid-18th century, Brocklesby performed some of the first scientific studies of the use of music to treat mania and other mental ailments (31).

When music is used in the clinical setting to achieve a health-related goal such as symptom management, it is called a music-based intervention (MBI) (32). Recorded music listening interventions (RMLIs) are a widely requested type of MBI in critical care units and can be facilitated by nurses without specialized training (33-35). The use of RMLIs to manage pain

and anxiety appear in several summary recommendations as accessible, acceptable, low risk interventions to promote safe and effective analgesia and anxiolysis in critical care (14, 32, 36-38).

Prior studies examining the use of RMLIs in critical care and among MV adults suggest that RMLIs may be effective adjuncts for the treatment of pain and anxiety (39, 40). However, most clinical trials of RMLI in critical care suffer important limitations threatening their generalizability. First, despite recommendations to use patient preferred music for symptom management in critical care (41-46) most studies of RMLI in MV adults use music selected by investigators or limit patient choice of music to slow tempo Western classical or instrumental pieces even though jazz, country, pop music, rock and roll, and spiritual music have been identified by patients as 'preferred', 'relaxing', and helpful for pain control (47). Lack of participant diversity is another important limitation in North American studies of RMLI in MV adults in which 87% of participants identify as white. (48-51). Given the known variations in music preference and familiarity associated with cultural background, age and context (24, 52, 53), inclusion of a more diverse group of participants may result in a wider range of selected 'preferred', 'familiar' music. Furthermore, racial and ethnic minority populations experience more psychological distress during and after critical care hospitalizations than their white counterparts (18, 54, 55) and may also experience RMLI differently. Examination of the perspectives of a diverse group of people can help inform the safe and effective use/integration of RMLI in a culturally diverse critical care population.

Finally, the majority of clinical trials examining the effects of RMLIs in critical care only explore outcomes of pain and anxiety. However, critical care symptom experience is complex. These sharply focused studies may overlook upstream causes of pain and anxiety such as fear,

communication deficits, and sleep disturbances or important symptom experiences such as dependence and loneliness not normally examined in critical care literature. Emerging evidence points to both short- and long-term morbidity associated with psychological distress in ICU, suggesting the need for an agnostic exploration of symptoms for which people use music in critical care. Soliciting the views of patients who have listened to music during their critical care hospitalizations through qualitative exploration may reveal a wider range of uses of music listening. Incorporating patients' perspectives is essential to the development of effective and clinically meaningful interventions (56). Therefore, the purpose of this study is to describe patients' perceptions of the effects of listening to self-selected music on symptom experience during MV after critical injury.

Methods

Theoretical Framework

We used Grounded theory methods to answer the research question. Grounded theory allows a researcher to build a conceptual framework of a social or psychological phenomenon based on the views, experiences and beliefs of the participants (57). The use of music as a therapeutic intervention is supported by two important theories, each based in the philosophical principles of holism: Antonio Damasio's Theory of Emotion, Feeling and Core Consciousness (27) and Florence Nightingale's Theory of Nursing (and the Environment) (58). Holism is a philosophy that emphasizes the connection between the body and the mind and acknowledges the inseparable relationship between the two (59). Damasio posits that homeostasis, and ultimately survival, are dependent on the relationships between physical feelings in the body proper, emotions developed in the brain, and consciousness, an outcome of the mind. According

to Damasio, memories, of physical and emotional perceptions, form a complex network of experiences unique to each individual, or a neural map. Music, a strong auditory stimulus, is processed in parts of the brain that are responsible for emotional regulation and homeostasis. Through music, people may access their own memories and be influenced physically and emotionally after injury and critical illness.

Most famous for her work detailing the interaction between person and environment, Nightingale also identified music as a powerful sensory stimulus enabling nurses to alter the environment surrounding a patient while providing individualized care, another important tenet of nursing. Like Damasio, Nightingale argues that wellness and recovery, are achieved through conditions which promote harmony of mind, body, and spirit, such as music. Finally, Nightingale recognized the complex nature of symptoms, arguing against narrow assessments of singular symptoms, and instead advocating for complete, holistic assessments. As such, Nightingale's approach to symptom assessment and management is well suited to inform a rich exploration of the ways critically ill and injured adults use music during their hospitalizations.

Setting, participants and study design

The setting for this study was a single urban, academic level-1 trauma center and safety net hospital. Inclusion criteria were: age 18 years old or older; current or recent patient or family member hospitalized in the surgical or neuroscience ICUs; having experienced MV during the hospitalization; and having listened to recorded music in the ICU as a patient or having played recorded music for patients in ICU as a family member. Participants for this convenience sample were identified and recruited in 3 ways: 1) as part of a concurrent prospective pilot study examining the use of RMLI during MV; 2) through referral from critical care clinicians who had played recorded music for their patients or observed their patients listening to recorded music

during their hospitalization; 3) through census review by one of the investigators (R.M.), who is also an advanced practice provider in this ICU. Purposive sampling was used to ensure a diverse sample of respondents and was ongoing until thematic saturation was achieved. Institutional Review Board approval was obtained from the Committee for Human Research at the University of California, San Francisco. Confidentiality and anonymity were maintained in accordance with their requirements.

Use of Recorded Music Listening

Recorded music was sourced and played through a variety of means including web-based subscription services (e.g., Spotify); streamed radio broadcasts; or from personal devices brought to the bedside by patients and their families. Unconscious patients listened to music through portable speakers placed near their hospital beds. Conscious patients used portable speakers or headphones depending on their preference. In general, families made music selections for unconscious patients. Once patients regained consciousness, they made their own selections. There were no restrictions placed on the genre, tempo, mood, rhythm, or lyrics of the music selections. Patients were allowed to listen to music at any time of day and for any length of time.

Data Collection and Analysis

Recruitment and data collection began in August 2020 and ended in November 2021. The primary source of data was a series of semi-structured interviews conducted by the principal researcher (RM). An interview guide was developed for the study (Appendix 1) and was adapted throughout the study period according to participant responses. All but 2 interviews were recorded and transcribed verbatim (RM); one participant declined to be recorded, and another pair of informants were only available to speak over the telephone. Interview transcripts were then rechecked against recordings to ensure accuracy. Detailed notes were taken during the two

unrecorded interviews, and summaries were shared with participants at the close of each interview as a form of member checking, and to clarify concepts. In addition to the interviews, field notes were collected by the principal researcher (RM) throughout the study period including quotes and observations made by clinicians, patients, and families.

All interview transcripts and interview summaries were entered into Atlas.ti 9.1, along with field notes made by the principal researcher (RM) during the study period. Data collection and analysis including memo writing and constant comparison was concurrent throughout the study period, as is consistent with grounded theory methodology (57). Word-by-word and line-by-line open coding of all transcripts, field notes and memos was performed by a single researcher (RM). Open coding was centered on actions (over nouns) to maintain context and rich description. Next, focused codes were created (Appendix 2) from the open codes and through overall impressions of the data. All transcripts were read and re-read by the co-investigators (HL, JHE, TB) who then validated the focused codes and assisted with axial coding through discussion of agreed on emerging categories and relationships between emerging themes. As themes were explored, transcripts and notes were again reviewed by the research team and analyzed for exemplars of the emerging themes and divergent cases, staying vigilant to distinct voices and contrary experiences. Individuality was maintained through illustrative quotes and exemplars. The analysis was deemed complete, once thematic saturation was reached, and categories and subthemes were organized into a coherent whole.

Throughout this process of reflection, co-investigators wrote memos and used journals to make note of their own perspectives on the stories they heard and the situations they observed, in order to remain aware of prior points of view and how this may be changing or influencing coding and interpretations. Memos, including observations, ideas connected to observations,

related thoughts and connections between ideas, data, codes and constructs were kept and included in the analysis. All data including audio recordings, transcripts, notes, memos, codes, early frameworks, and journal entries was saved. Member-checking (e.g., study participants) was ongoing throughout the research including during interviews in order to both sharpen understanding and allow for member corrections. As well, analyses and results were shared with key informants, members of the community and through peer review with critical care clinicians.

Results

Fourteen semi-structured interviews were conducted with 16 informants during the study period (Table 3.1). Interviews were conducted in person (n=12), over the phone (n=1) or via video conference (n=1). Interviews were approximately 40 minutes in length (7:45- 61:21 min:sec). Interview informants were a combination of patient-participants (n=7), family members of patient-participants (n=4), or both (n=4). Patient-participants were an average 36 years old (22-64). Twelve were hospitalized after sustaining critical polytrauma, including 7 who also had traumatic brain injury (TBI), and 2 people were admitted after a stroke. Four patient-participants identified as Asian, 2 as Black/African American, 2 as LatinX and 6 as white/European. All of the patient-participants were male; however, most family-participants were female. All but one subject spoke English, and for that interview a certified interpreter was used for translation into Spanish. Thirteen interviews were conducted during the hospitalization, either at the bedside in the ICU or in private rooms on the medical surgical floor. One interview was conducted 7 months after admission. In addition to the semi-structured interviews, the primary investigator (RM) documented statements and observations about the use of recorded

music in critical care made by other key informants such as patients, families, and staff. (Appendix 3.3).

Music selections

Overall participants expressed enthusiasm and gratitude for the offer of and use of music during their ICU hospitalizations. Selections were made by family members (n= 7), patients (n=4) and a combination of family and patients (n = 3). Music selections varied widely across the group and within the participants. Though not formally catalogued, examples of several of the music selections are presented in Table 3.2.

Themes

Six themes emerged describing the ways participants felt listening to recorded music affected their hospital and symptom experiences (Table 3.3). Participants described that listening to recorded music: 1) Restored their consciousness; 2) Maintained their cognition; 3) Humanized their hospital experience; 4) Provided a source of connection; 5) Improved their psychological wellbeing; and 6) Resolved the problems of silence.

Restoring Consciousness

Both patient-participants and their family members described the use of music listening to restore consciousness after anesthesia, traumatic brain injury, sedation, delirium, and stroke. Music served as a trigger to awaken an otherwise quiet, unconscious mind.

> *…it definitely brought me out of that little coma or the little sleep I was in. Like it just shook me and was like 'Hey Buddy'… 'Now's your time'… 'You're up! You're here. You made it!' … it was … <u>waking</u> me up it was bringing me home. And I felt I was far away. (P7).*

Others felt that music was encouraging them back to awakeness. One participant explained, *It's like music it's telling you "Hey, you belong in this world, don't drift away to somewhere else".*

Like 'specially people in coma. Like "don't drift away to coma". Like 'you belong here. You need to wake up'. Eventually.' (P5)

Patient-participants wanted to be conscious. For many being conscious was a way to reassure people of their survival, and many felt that listening to music helped them accomplish this. *I remember thinking I really wanted to wake up… I would like to think it brought me, uh, brought me back…music saved my life' (P11).* This perspective was echoed by many who saw listening to familiar music as a way to '*bring you back'* after coma, to *'stimulate the brain, wake them [sic] up'* (P10). Participants explained that listening to music stimulated the recall of their memories. *'Yeah- all your memories just come flooding back in, with those brain cells and music' (P7)*. The memories associated with music served as a a '*trigger*' that helped to '*jumpstart*' patients' consciousness.

> *But to me I guess...it just kinda sparks…umm…sparks some…mind…creativity? Mind…not control but some type of state where you're reminded of what your life was like, or what your life is. I would like to think it…made me wake up…*

Family members also chose music associated with their loved ones' life memories, with an aim to help restore consciousness through music-induced memories.

> *we had these memories with my dad…you know these songs either played [or were] playing the background… I think we were all just hoping that … those, you know those musics , would trigger memories for him- the same memories that we have with him, and … just kind of getting him to come back to us…I think that's that's what we were really hoping for and saw (FP1)*

Familiar music was, for many, an accessible sensory lifeline, a meaningful stimulus which people could '*grab hold of and use'* to pull themselves out of a *'fog'* into a more conscious, awake and aware state. One man explained,

> *'…it definitely..pulled me out of my like submission because I was just I just wanted to sleep and be done with it and … hearing the music it was like waking me up because it*

was familiar and it was something that I know and I love' … because I was in such a, a f'f'f' a flimsy state that when I heard that music, I was just like 'I'm here, I'm alive', and I was fighting to get back to being awake and conscious (P7).

Clinicians and family members also observed more wakeful states and signs of improving consciousness associated with listening to music including seeing patients who had been comatose smile, bob their heads to music, and tap their feet. In one instance a previously non-interactive patient scowled at the staff when they removed the tablet used for playing music, and followed them out of the room with her eyes, staring at them until they replaced the device. One family member described the moment when she saw the first signs of her father's emergence from coma,

…one of the days when I went to visit my dad, [I was] just having conversations with him … recalling my wedding and about how … we danced at my wedding and this song played and asking him whether he remembered and at that time …he was, limited in his communication to just head nodding but I could see him... there was something in his eyes that sparked something and you know with him nodding his head too, it's like OK he's coming back he's coming back and I really do think that, you know, hearing some of the music did help. (FP1)

Maintaining cognition

Listening to music was seen by many as an accesible form of cognitive stimulus even during a coma. One family described how they hoped to engage their loved one's brain and stimulate thought processing while recovering from a stroke by playing familiar music.

to hear something that's familiar… that will trigger their memories of something as their body is recovering from whatever trauma that they're going through……memories of growing up maybe trigger something in his brain or something maybe hearing it …Maybe certain songs will trigger memories of, you know, 'oh where was I at that moment when I heard this song, you know? 'what was I doing' or 'who was I with'? And maybe that will help trigger things, you know, like when he hears different songs that that's being played (FP9)

Memories triggered by listening to music served as both as a starting point, to initiate awakening, and as a guide by which to traverse from coma and confusion to alertness. One man

explained, '*a familiar song can take a person from a place of extreme confusion and unfamiliarity to a safer, kind, happy and ultimately familiar place'*.

The use of sedatives was disorienting for many and left them feeling confused and scared. Some used familiar music as a shepherd to navigate through this challenging experience. For one partcipant, the experience of sedation was frightening, *'the world and your, everything else you know is kinda flipped upside down…it can be quite kinda scary…I seemed to be in my purgatory a little bit…'.* But music helped him to move through it safely. '*I really wanted to be able to put some music on…to push me into… exiting …that space, or that k-hole, or whatever it was, in a positive way, you know, rather than being- rather than being scared.' (P12).* Others, who experienced hallucinations and delirium, used music listening to make sense of their surroundings, and ground their perceptions in reality. For example, one person described their hallucinations as '*less jarring*' when the music was playing.

Participants also reported preserved cognition through the use of music listening. One participant explained, *'Like I have, I have a clear mind, I don't know if that's due to the music or not, but like when I first wake up, uh…I am confused a little bit but, like at least I know what's going on…' (P5)*. These cognitive outcomes were noticed by family as well. One woman described her father's improvement after a stroke:

> *The difference that I saw in him, was his cognitive engagement. …It's one thing that we were there holding his hand, but seeing something you know spark in his eyes, and him kind of raising his eyebrows, like…he KNEW something… especially at that time when…sometimes it was hard to know whether he was there- to see him get engaged and you know cognitively wake up a little bit, I think that's that's what I saw* (*F1*)

This observation was echoed by other friends and family who marveled at a loved ones' cognitive abilities after TBI.

> *I've been just blown away by his cognitive… function. Like, it's just- he's, he's- it's completely not noticeable! But like that seems crazy to me, that he got hit his head so hard and there was bleeding in his brain, right, and all that and he's just…I mean, I know he's very resilient, but that's just, that's part, that's just blown my mind (F11)*

One mother observed about her adult son that his level of conversation and ability to construct careful arguments was surprising despite having a TBI, and attributed this to having listened to msuic *'Four days after a traumatic brain injury… that trait has, has come through again….he didn't lose that with this horrible accident. That's the thing that's absolutely phenomenal. To hear him talk like this.'(F14)*

Humanizing the hospital experience

Patient-participants, family members and staff all saw the use of recorded music as a way to humanize the ICU experience by restoring important facets of humanity such as personhood, identity, personal history, control, independence and addressing a mechanized environment. Music reinserted personhood into the clinical space. Playing recorded music for patients helped to remind clinicians that patients were human beings, pushing staff to see past their diagnoses and the mechanistic environment surrounding them. One nurse explained, '*Patients are people- music adds to that… we get very disease focused, see trauma, see disease, this [music] shows people [for who they are]*'. One resident physician offered that hearing music in a patient's room '*humanizes him to me'.* And one man recovering from critical poly-trauma explained that prior to the offer of music, all of the human contact he experienced had been disease and injury oriented. When staff offered to play music, he finally felt they were seeing and treating him as a *person*. Similarly, playing recorded music for her father helped one woman assert *'that he wasn't just a patient, he was someone who… was HIM... and that they're all these pieces to him that are important' (F1).*

Patient-participants described music selections as closely aligned with their identity. Despite residual deficits after a serious TBI, one young man was immediate in his selection of a preferred song, using it to get his '*groove back*', to feel more like himself or '*at base*'. He explained that '*music has a…. property that is …. very … specific to … your identity (15)'.* Music was usually chosen by families, but in one example, a group of clinicians of similar age and background to a young, comatose man suggested a playlist after looking at photographs of their patient brought in by his family. The song choices delighted his family, who felt the staff had seen their brother for who he was, and identified with him. They laughed as clinicians and staff danced along to the [sometimes] explicit lyrics. Later they explained that asserting identity through personalized music was a form of advocay. *Hopefully, if he hears it he knows that… people are thinking of him… because [the music] is so individualized to his personality, what he likes, you know he knows that, 'Oh, you know, maybe someone vouched for me'(F9).*

Through the memories attached to music, people were reminded of who they were before their hospitalizations.

> *when you ask me what kind of music do you like?- that gave me a chance to remember the good times, … the relationship with the prints of my heart. I remember the good times, the good times in my life when I was listening to the music ...yes, yes it's made me think… it made me relax …the memories…I appreciate- that you givin' me that. (P17)*

Others described the feeling of being 'brought back' to themselves with music after life changing trauma. *'It was just like more of just bringing [name withheld] back to [name withheld]. Yeah … it definitely just brought me back to.. ME and MY ROOTS…how I believe and how I see MY music and my positivity.' (P7).*

Not all memories invoked through music were positive, *'Its always, its always going to take you back …to a place that you know… it's like a fast track to all of the emotions that link to*

that music and the experiences that you have to those songs. So all of the good times and the bad times' (P12). These potent facets of identity were cherished nonetheless. *'Familiar music is like an old friend. Sometimes they're good sometimes they're bad… but whatever it is it's yours.' (P5*).

Alongside indivual memories, people associated music with their family identity. This was reflected in the choice of music by both families, and patients. People desribed their music choices as symbolic of their 'childhood', or memories associated with their parents, siblings, and grandparents. Others were reminded through music of their neighborhoods or places of origin through music. *'It was my mom, my dad and also my hood, like, in the streets. We would always have a speaker playing…you'd go outside with music, and go inside- my neighbor's playing music' (P8).*

Threats to identity left one man feeling that death was near; for him, selecting music steeped in family history was a natural choice. *'I felt like I was on like my ancestral plan, like I felt like my body and spirit were in two different areas. So when you asked me, I was already with my grandfather and I was already standing next to my brother.' (P7)*

In addition to reasserting personhood through identity, music helped patients to feel more normal. Several participants described music as an essential facet of their every day life. *'Music is something that is always been really, it's been my way of living, it's the way I live' (P8)*. Some asserted that music was a 'need'. *'I think, like that no matter what you do… music it's something that's so important in your life that you always need.' (P5*).

Facing life threatening events, and cast into chaotic settings patient participants used music to normalize their environment. One family member explained, *'It was introducing, not normalcy, if you will, because this was just ….a horrendous event, and I think introducing music*

that you're familiar with, or even not, but just music…would bring more… normalacy, normalacy to the whole environment. And I think … you needed that.' (MP14). Restoring some feeling of normalcy helped people resituate. *'I've listened to the same songs like millions and millions of times in different situations, so it just, it's something that is just so familiar to me and … it helped me just normalize what was going around me.' (P8)*. This view was shared by others who used music to regain a sense of normalcy in an unfamiliar environment.

> *At least play some music, for people that just woke up you know like they can, they can relate to something at least and they can at least feel normal. Like me, the biggest challenge was, after the accident, I don't feel normal again. And I would- after-… when I am listening to music at night when I'm sleep- like trying to go to bed, I feel normal. I feel like I'm I'm in my bed, in my home bed! You know like I'm just listening to the music, relaxing and trying to go to sleep. Instead of like hey like it's a room like I am trying to leave you… (P5)*

Mechanistic sounds were a constant reminder of the trauma experienced by this group, threating their humanity. Several described feeling re-traumatized by alarms and oppressed by the unatural sounds of humidifiers, pumps, and machines. One participant used music to distract himself from the tube feeding pump which he found upsetting.

> *The nurses are giving you medicine, through your nose- you can, you can hear the- you can hear the machines are feeding you through your nose…that's just disgusting. That's why I told them so many times, I don't want the feeding tube…. I don't want …the feeding pump. I told them so many times, I don't want it. Like all you can hear is the feeding tube. You can hear and you can feel that something is pumping into your stomach. It's just disgusting. You don't know what's been pumping into your body' (P5)*

Normalcy achieved through music helped people begin to heal from their injuries and emotional pain. *'I felt like I had to have a certain sound in order to be able to get over certain traumas or even get over this accident. I felt like music uplifted me…it brought me back. I feel like music brought me back to me feeling normal.' (P8)*

Loss of control was another threat to the humanity of patients in the ICU. Choosing and playing music softened this experience. As one young man explained, music *'made me feel little bit safer being being able to listen to the sounds that I can control' (P8).* Similarly, one woman hoped music would ease her husband's loss of independence in ICU. '*He has been in control his whole life and the frustrating thing is that he can not move around … can't talk… and that's where this music stuff comes in' (FP3)*. Some recalled bad memories of being restrained in the ICU. One man wished for music to help distract him from this ultimate loss of control. He explained,

> *That's a really really bad feeling. You know like when you first wake up from ICU and … like you're tied down, you're confused- like you're just there 24 hours a day- it's a very bad feeling….it feels like- it's worse than prison….like your body's hurting… But, you know, something else like music to distract you would be a better option…instead of, you know, getting restrained, and like just hating it. (P5)*

Choosing and listenig to music also presented an opportunity for participants to assert some control and independence. One young man with a traumatic amputation explained,

> *you're not in control of anything when you're at the hospital….everything is your doctor, your nurses…. everyone is telling you what to do, so I feel like it would help to have something that you could do on your own that you, you know, like, that you have complete control over, so that would be the music. Like, I would want to be able to listen to my own music, on my own time, when I want…that's, like, something that I could do. I could do it. Like, you know, I might not be able to walk, I might not be able to see…but I'm able to change the song. I'm able to choose a song you know. Music, makes you feel a little bit like not every- I'm not being controlled by by by this aspect, you know, because at the hospital I feel like everything is very controlled. The way we eat- the time limits, everything is, like, everything is a schedule. (P8)*

Regaining some control through the use of music also helped people assert themselves.

I feel like music..helps me just remember myself that I'm still independent. I'm still my own person. I could still make my own decisions. I could still play my own song'. (P8)

Providing a source of connection

In addition to feeling dehumanizined, patients in this cohort experienced fear, loneliness, and lack of social connectedness. Listening to music facilitated connection for patients to their families, their environment and their personal histories. As explained by one man *'my grandfather used to say that human beings are social creatures, and we can communicate through music and I firmly believe that' (P10).*

Listening to music gave people a way to connect to their families when restricted visiting policies kept them apart. *'My family can't be around me in the room sharing with the love. So I felt the love through the music because of that connection that I made with the music.' (P7).* Listening to music invoked memories of life outside the hospital, including times when people listened to music together. This was expressed by several family members who hoped the music would lessen the loneliness of hospitalization One explained,

> *the idea of… your friend being alone in a hospital seems pretty horrible, so just the idea of any music in there-The idea of him just being in a hospital room by himself…alone. It sounds horrible. It's like very lonely too. And so the fact that there was music definitely made it seem nicer (F11).*

Several participants complained of the feeling of time standing still, a psychic doldrum which exacerbated feelings of loneliness and separation. Listening to music helped to moderate this experience

> *… some people don't have their families here and you're just looking at the time, you're just looking at clock all the time waiting and seeing time pass by and you feel alone. Yes music helps. Music helps because you don't feel alone (P2).*

For another man, missing his family, listening to music was *'kinda a little bit of a connection to home' (P11).* Others compared the benefits of music directly to those of a visitor, *'Having a visitor is the like music- let's your mind wander to someplace else… helps you.. get*

through the day' (P10). Listening to music was akin to '*hearing another voice'* for one young man, a form of socializing. He explained, '*the chord progressions speak to you'*.

Patients were in search of connection, something to '*grab hold of*' psychologically and cognitively. Listening to music provided a means for people to connect with their environment and circumstances despite being intubated and unable to speak.

> *I think that it should be a like a family question, like what type of music do you guys listen to because it <u>does</u> help you connect when you can't say nothing, your mind is still processing these items and and attaching music to your happy moments in life you know (P7*)

One man suggested that music could even serve as a form of connection to people in coma, *"they tell you to talk to them, touch them. Because they want that connection. So I think music can provide that connection for them' (P5)*. Hearing familiar music also helped people to feel cared for by, and connected to, the clinicians looking after them. One man explained that hearing familiar music **'***might help me think that you know like I'm belong…I'm belong to, you know, like, belong to this nurse… like not belong to somewhere else… like belong to…here'*.* (P5).

Critically, familiar, personal music helped people connect with themselves.

> *cuz we coulda easily put some hip hop on, and just drowned the noise out. But for me it was more like, I wanted, I wanted something to connect with and to <u>empower</u> me and I know that you know I'm ALIVE and being alive I felt closer to my grandfather, closer to my brother… (P7)*

Improving psychological wellbeing

Participants described the use of music listening to address several aspects of their psychological wellbeing during their ICU admissions including: taking their mind off their problems, managing intrusive thoughts, processing emotions, accessing resilience, and experiencing hope and pleasure.

Several people requested music during periods of extreme distress (anxiety, breathlessness, frustration). For some, the choice of music was not important. Several participants suffering intense agitation or anxiety asked for staff to play '*anything*', claiming '*it don't matter*'. People who had been trying to climb out of bed for hours relaxed almost immediately once music was started in their rooms. One young man nodded vigorously when clinicans asked 'should we restart the music' after he started to cough and sit up in bed despite high dose sedation. Later, some explained that listening to music had helped them by giving them something other than their suffering to focus on. One person said, *'I think I was looking for, like, a distraction? … so it's like something to pay attention to, other than my own pain or whatnot (P14).* For some, music was a '*mental escape*' from being trapped in a hospital. Participants explained that music '*eases*' and '*soothes*' by *'replacing [sic] all the things that you have in mind".* This view was endorsed by a young father who had sustained a life threatening injury.

'Strapped to the bed, tubes everywhere- and it [music] just made me feel like nothin', none of that was important you know? The music was just playing and soothing me and it just made me not think about all my all my other problems I had right at that moment'. (P7)

Most of the people in this group suffered the progression of time. As time stood still, people felt worse emotionally. *'Time was just, like, time was dragging on. Pain was higher. I was, like, just in a worse mood, more depressed' (P12)*. Listening to music gave them something else to focus on. One participant explained,

> *the feeling of the progression of time. …like [the] hallucination loops or whatever, [were] very unpleasant. I was just playing a game where I would get points by breathing… I knew I couldn't fall asleep and so I was just waiting to get better pretty much… and come off the ventilator and so…I'd like…'breathe, breathe, breathe'… and every time … I'd just have this… mental…little video game that I'm playing where I just*

> *get points by surviving…I think the music provides like an alternative way of…focusing on, like I could just do, I could just breathe and I wouldn't have to worry about having to, like…meticulously keep track of how many times I'd breathed. (P14)*

Unfamiliar environments and uncertainty about the future left many feeling scared. Listening to music helped one man '*feel a way that I wanted to feel that was, like, safe.'* (P8). Many reported using music to manage intrusive thoughts. One man explained that music *'put[s] people…in more of a meditative state which isn't a bad place to be rather than… flashing through whatever trauma they've been through'. (P12)*. One man used music to get relief from thoughts of his accident. For him, music '*took away the accident, …it took away my hundred percent of seeing everything back to back to back.'* He explained, *'it relax my mind. Cuz' my whole, my whole mind was thinking about the pain and my trauma… When that thing played it took my pain, it took my pain and 'cuz it shifted my whole position from the, from the accident….So that helped me, that helped me.' (P17)*

Flashbacks interfered with sleep for many, but listening to music helped participants to get rest. '*when I was listenin' to the music - put my mind at ease- and I went to sleep listening to the music …. I went to sleep- even for a long time in my sleep I was listening' (P17).*

Several of the participants in this cohort experienced significant loss associated with their hospitalizations. Listening to music facilitated emotional processing of their experiences, allowing them to begin to heal psychologically. For some, listening to music was a comfort during a time of grief.

> *Like let's say, like, you know, my accident. You know, there's pain…that pain is… coming from... why it happened to me, losing a leg. You know so it's painful. It's painful. It's very, very painful to know that my life is gonna change drastically and I didn't want it to change drastically. Its like music … it's giving me a hug.(P8)*

Others described the use of music to stimulate tears. '*Like, when you listen to a sad sad music, like you would want to cry, the tears sometimes come by itself, right?'* Emotions conjured by music gave some people a way to express their sadness. One young man explained,

> *There is a song called Insha Allah.... When I was in ICU if you guys had played that music …I would probably feel a lot better… Yeah especially Muslims… when they listen to this song…like when they are in ICU and all alone, like 90% of them will probably cry. You know it's, it's a song that really touches your heart. And it let goes of a lot of anxiety, it let goes of a lot of stress (P5).*

For those who were unable to talk about the troubles they were facing, listening to music was a way to start to process grief. Two friends described the first moments they spent together in the ICU, '*we just sat there and listened to music together… We didn't know what else to talk about. So, we just listened'* (P11). Others experienced a numbness after their injuries. One man described how hearing music facilitated feeling again, allowing him to re-engage with his psychological experience of trauma and access his own resilience.

> *I think it changed how I felt about myself in that moment. I, I was like I said- when I was on the operating table and I came in the ER, I felt I gave up already, I didn't think I was going to come out of it …I still didn't process anything like, it was still very much numb and blank and ….when I started to process my own thoughts and and my own feelings it was when the music came on because it was it was attached to me and it was what I wanted. (P7)*

In addition to quieting instrusive thoughts, and comforting the griefstruck, listening to music gave people hope and enjoyment. Hearing music reassured patients that no matter the physical outcome of their trauma, they would still find pleasure in life. *'… as soon as you know that your ears are working, you know whatever physical thing you're going to be left in, you're gonna be at least, you know, enough to still enjoy what you love' (P12).* Even in the ICU people described music as filling their 'hearts with happiness'. Family members observed that music 'brightens up the space'; they hoped that playing and listening to music would bring joy to their loved ones. And it did. One man explained that while his days in the ICU were 'the worst days of

his [sic] life'- he 'did remember… enjoying the music'. Others endorsed that listening to music gave them something 'fun to think about'. For some people, music brought 'inner peace'.

> *To hear something familiar gave me something to look forward to when I was already at the end of my chain. Like I, I had already accepted that I was dead and I didn't think I was going to wake up … but then I knew that there was ONE thing that was familiar … and I was just like YES, thank G-D, that's my song right there! (P7)*

Resolving the problems of silence

Silence was seen as problematic by most participants and their families. Without sensory stimulus, people worried that their loved ones would not be able to connect to their environment and would be stuck without a means to emerge from unconsciousness. One mother of a semi-comatose young man observed: *'he is just sitting here in a blank room, you can't just be in a blank room, that isn't healthy'- [there's] nothing to come back to'*

Silence was seen as a form of abandonment to those experiencing coma. One patient explained:

> *I think, like a lot of people in coma, people just left them there, you know? Like people just left them in silence. They shouldn't do that. Talk to them, touch them, you know, let them feel. Even if they don't feel anything, like play some music at least. Like let them know that, hey we're calling you…We're calling you from here. Uh, you need to come back. Yeah, I think people appreciate that… a lot. (P5)*

Silence was associated with restraint, described as something to endure.

> *I really wish that when I first wake up in the ICU, like when I was confused and you know like the nurses has to restrain my hand for a little bit… I really wished somebody had played some music for me instead of just lying down there like you know in silence… when I was in the ICU my hands were restrained and I was lying in silence and that's not a good feeling. (P5)*

Other family members observed heightened fear response in their loved ones in silent, quiet rooms. *'It was so silent that everytime someone bumped a table or something… [it was] starling…. His eyes would get wide…why is it so silent'?* One patient used music to moderate the

sudden sounds of doors opening, monitors beeping, each which triggered intrusive thoughts of the trauma he endured. *'…it helped me come up from- a little noises at first- because I was thinking and thinking- why me, why me all that time' (P17).*

Silence was also associated with depressed mood and dampened hope. One pair of sisters noticed a more 'upbeat' staff and joyful ambiance when music was playing as compared to the sterile mood experienced in a silent room. They wondered if this change in atmosphere might not help encourage their brother to recover.

> *Uh, you know it's just so like quiet here …[the music makes it]… seem a little more upbeat and not so quiet… [it] feels a little bit more lighter, given the-the serious situation….it is a very serious situation, but if people are more positive, and if their tone could be a little more positive maybe that will also help him…their tone seems a little bit more healthier so maybe-like- he might feed off of that or he might feel it (FP9)*

People worried that their loved ones would feel disoriented in silence, adding that hearing music upon awakening may help a person to re-situate.

> *I think just not hearing silence or just not hearing maybe unfamiliar sounds, if you know, because he wakes up, he might not be like aware because he's not opening his eyes, you know? but just hearing familiar sounds I think might might bring something some kind of comfort to him if - you know -and during this time unsure when he might be unsure of where he's at (FP9)*

Discussion

This study provides important insight into the potential benefit of recorded music listening in critical care by identifying six previously undescribed uses of music listening in critical care: restoring consciousness, maintaining cognition, humanizing the hospital experience; providing a source of connection, improving psychological wellbeing and to resolving the problem of silence. Social and demographic patient information and music selections varied widely in this study, however the perceptions of the benefits of recorded music listening were

consistent. Overall, listening to recorded music helped participants to achieve psychological and cognitive homeostasis across a spectrum of arousal and emotional states. On the one hand, music stimulated consciousness and awakening, on the other, music lulled an overactive mind. Listening to music facilitated emotional processing for people experiencing numbness, but also distracted those burdened by fear and flashbacks.

Memories associated with music served as a stimulus for consciousness and cognition, but also facilitated psychological wellbeing during ICU hospitalization. Music-related memories contribute to autobiographical memory helping us to make sense of our environment, and to construct a feeling of identity and continuity (25, 28). In our study, a diverse group of participants used music to regain control, assert their identity, and reconnect with their environment. Playing and listening to patient-selected recorded music gave people a chance to be seen and accepted by the health care team as individuals, strengthening the relationships between patients and clinicians. Descriptions of these phenomena add to understandings that explain the mechanism of action of music listening for symptom management in critical care.

Music Listening for Psychological Symptoms

Few participants described the use of music listening for management of pain or anxiety. Instead, results of this study indicate that the potential uses of music listening are much broader and include important symptoms for which there are few treatments available, specifically to address *psychological* pain. Alone with their thoughts, many participants experienced hallucination, fear and flashbacks. While some participants agreed that music helped them to feel more ‘relaxed’, the mechanism for this was cognitive, through distraction. Preferred music was able to hold their attention, replacing the negative thoughts which had previously overwhelmed them. Relief from a racing mind also enabled some to get sleep and may explain improved sleep

experiences associated with music interventions in critically unwell adults (60). In other instances, listening to music gave traumatized participants a tool to process their emotions, a critical step in managing PTSD (61), common among ICU survivors.

Consistent with prior studies, patients in this group also experienced loneliness, de-humanization, dependence, and loss of control (6, 18, 19). Listening to recorded music helped people to endure these physical and psychological restraints. Feelings of powerlessness and loss of independence are threats to resilience, a predictor of PICS (62). Participants asserted control of their environment and thoughts when making music selections that made them feel normal and capable. Critically, being able to play personally selected recorded music helped participants to be 'seen' by clinicians and feel respected. Despite research asserting the value of family presence to prevent delirium (63), strict visitation policies limit patients' contact with their families, leaving them few options to engage in meaningful social contact. In our study, when listening to music, participants summoned their social lives through reminders of their living family members, ancestors, social events, and day-to-day habits. Many ICU survivors suffer from depressed mood, and sadness is a commonly reported symptom during ICU hospitalization. We found that, in addition to mitigating emotional pain, listening to recorded music may also augment positive feelings such as pleasure, joy and hope, and facilitate coping. Participants in our study reported that when listening to music they were reminded of happy times and felt motivated to survive. While there are no validated measures for many of these symptoms, aggregate instruments such as the Intensive Care Psychological Assessment Tool (IPAT) (64) and the Profile of Mood States (POMS) (65) may serve as proxy measures for future studies of RMLI designed to prevent and treat psychological distress in critical care.

Music Listening for Cognitive Stimulation

Prior works exploring the use of music in critical care have examined the use of music listening as a sedative. Rather than sedate, music listening helped unconscious participants in this group to wake up. This phenomenon aligns with recent research demonstrating improved level of consciousness after music intervention among people experiencing coma (66, 67) and TBI (68). Our findings are some of the first to describe the subjective value of consciousness for patients experiencing critical care hospitalization. In our study, people fought to regain consciousness, preferring an awake state to a sedated one where they had little control over their thoughts, bodies, and environment. Once awake and conscious, participants used music to process their trauma, situate, take control and to connect.

Findings from this study also contribute to research that explains the mechanism of action of music listening for symptom management in critical care. People in our study described music as a 'trigger', a recognizable stimulus to their consciousness. This is consistent with studies that show listening to music engages a vast bi-hemispheric network related to attention, semantic processing, memory, sensori-motor and emotion (25, 28). For example, the dorsal medial pre-frontal cortex is activated while listening to familiar songs. This phenomenon has also been observed in comatose adults who, after listening to music, showed increased evidence of semantic recognition on functional MRI after listening to familiar music (69).

Participants also attributed their cognitive agility to the use of music listening in our study. Listening to music, even during coma, may enhance cognitive recovery by keeping brains cells 'in use', a critical component of neurogenesis (70). Data demonstrate that the plasticity of the central nervous system may benefit from a rich stimulation regimen (71, 72). In fact, improved cognitive functioning has been associated with the use of music and music therapy

after brain injury (73, 74). In order to be of benefit for neuro cognitive rehabilitation, some argue that sensory stimulation must be organized, (e.g., music), and caution against sensory bombardment (e.g., alarms, mechanistic sounds) (75). While much has been written about the risks of noise in ICU, few have examined the risks of silence, isolation, and sensory deprivation in critical care. Sensory deprivation is a known risk factor for delirium in ICU (76) and is also associated with diminished brain plasticity (77). Sensory deprivation is also associated with isolation after TBI and may compound the negative effects of injury (77). Current clinical models of critical care favor sensory regulation limits, but purposeful sensory stimulation may be better for brain health (71). Listening to music, even during coma, may be enough to engage a mind otherwise threatened by lack of stimulation, ultimately preventing delirium. Listening to music also helped people to manage the confusion of hallucinations and disorientation associated with sedatives, traumatic brain injury and delirium. Participants in this group described feelings of abandonment and restraint associated with silence exacerbating the stress of their hospitalizations. Here too, playing music moderated these experiences. Stuck in an isolated, mechanistic environment, participants used music to pass time while connecting with their identity through memories invoked by the music.

Limitations

There are several limitations to this study. First, all patient-participants in this study identified as men. Interviewing a more gender diverse group may confer new insights into the symptom experience and use of music during critical illness. Notably, several of the other informants in this study were women, whose views were consistent with the interviewed patient-participants. Similarly, all participants in this study were admitted to a single, urban trauma center. Since the culture of critical care units varies, including perspectives from people

in other centers would add to the understandings developed here. Finally, this study was conducted during a period of severely restricted visitation and societal stress related to the Covid-19 pandemic which may have heightened the experience of isolation, and loneliness described by the respondents. However, both problems have long been reported in critical care, and the insights gained through this research are likely to be of help to many whose loved ones are not able to be with them for other reasons.

Conclusion

We believe this is the first study to describe the use of recorded music listening to manage the psychological symptom experience of ICU hospitalization. Our results suggest that music interventions may have an effect on cognition, confusion, intrusive thoughts, sleep, fear, loneliness, helplessness, and loss of control. Participants used music listening to take control of their thoughts, their bodies, and their environment. While the symptom experience was diverse in this group, common amongst all was a desire to achieve cognitive and psychological homeostasis. These findings add to the growing understandings of the mechanism of action of music as a meaningful cognitive stimulus and help to develop a framework for understanding how music works to help people recover from critical illness. Delivery of recorded music is an equitable, patient-centered intervention that can easily be tailored to individual needs. Given the prevalence of long-term cognitive and psychological morbidity experienced by ICU survivors, recorded music interventions designed to treat psychological distress are likely to be of great benefit.

Appendix 3.1: **Interview Guide**

1. Tell me how you came to choose the music we're playing for [insert loved one's name]?

2. Describe some of the times [insert participant's name] listens to or play music at home? In life?

(*Probe: describe some different scenarios when they listen to, play, or use music in their lives.*

Probe: describe their relationship with music

Probes: do they play an instrument/DJ, do they work with music or study it?)

3. How would you describe the music you chose?

4. What do you think is going through [insert loved one's name]'s mind right now?

5. What sort of symptoms or feelings do you think [insert name] is experiencing?

Probe: do you think they are uncomfortable?

6. How do you think this music will affect [insert name]? Physically, emotionally?

7. And how do you think music works on people?

8. How does the music experience change between the hospital and home?

9. How has music influenced your views of this hospitalization?

10. How, if at all, has having a music choice influenced your views of this hospitalization?

11.If you had to rate the music on their play list on this scale (*use visual analogue scale*) of 1-5 with 5 being very personal, and 1 being not so personal, how <u>personal</u> is this music selection to [insert participant]?

12. What about <u>familiar</u>? How familiar is this music for [insert participant] Same scale, is it extremely familiar or not so much?

13. And, what about <u>preferred</u> where 5 is all the way in their favorites and 1 is not liked at all?

14. How do you feel about music? Can you describe your own experiences and history with music?

15. What is one thing you want to tell me about the study of music and being in the hospital?

Table 3.1: Description of Participants and Interviews

Participant	Sex	Age	Race or Ethnicity	Place of Origin	Languages	Religion	Employment	Housing	Diagnosis	Injury	Informant	Interview (min)	Location
1	Male	55-65	White	Western Europe	English Hungarian	Catholic	Self-Employed	Housed	stroke	NA	Daughter	34.00	Home
10	Male	20-30	Asian: Japanese Filipino	California Hawaii	English	NA	Unemployed	Unstable Housing	Critical poly trauma with TBI	PVA	Self	45.00	Ward
5	Male	20-30	Asian: Uyghur	Mainland China	Mandarin Turkish English	Muslim	Employed	Housed	Critical poly trauma with TBI	MCC	Self with partner	42.03	Ward
8	Male	20-30	LatinX	SF Bay Area	English Spanish	NA	Employed	Housed	Critical poly trauma	Assault PVA	Self	50.06	Ward
11	Male	20-30	White	Midwest USA	English	NA	Employed	Housed	Critical poly trauma TBI	PVA	Self	48.40	Ward
12	Male	35-45	White	Western Europe	English	NA	Unemployed	Unhoused	Facial/airway injuries	GSW	Self	41.54	Ward
13	Male	20-30	Black African American	SF Bay Area	English	NA	Unemployed	Unhoused	Critical poly trauma	GSW	Self	7.46	Ward
14	Male	25-35	White	Canada	English	NA	Employed:	Housed	TBI with facial trauma	BVA	Self with family	61.21	ICU
17	Male	45-55	Black African	Northern Africa	Ethiopian English	NA	Employed	Housed	Facial and airway injuries	GSW	Self with spouse	20.54	Ward
7	Male	25-35	Asian: Filipino	SF Bay Area	English	Catholic	Unemployed	Housed	Critical poly trauma	GSW	Self with family	50.51	Ward
2	Male	25-35	LatinX	Central America	Spanish	Christian	Unemployed	Housed	Critical poly trauma	GSW	Self	8.42	Ward
3	Male	60-70	White	West Coast USA	English	NA	Employed	Housed	Critical poly trauma TBI	MVC	Spouse with family	45.00	Phone
15	Male	20-30	White	SF Bay Area	English	Buddhist	Unemployed	Housed	Critical poly trauma TBI	GSW	Self	15.52	Ward
9	Male	30-40	Asian: Filipino	Philippines SF Bay Area	English	Christian	Unemployed	Housed	stroke	NA	Siblings	19.12	ICU

Key of Abbreviations: NA: Not applicable; PVA: pedestrian versus automobile crash; MCC: motorcycle crash; GSW: gunshot wound; BVA: bicycle versus auto crash; MVC: motor vehicle collision; TBI: traumatic brain injury; Med Surg: medical surgical unit; ICU: Intensive Care Unit; SF: San Francisco

Table 3.2: **Music Selections**

Participant	**Music chosen by**	**Music Selections**
1	Family	Brahms, Hungarian rock of the 70s, Pop Rock (UB40, Beatles) Radio: 'The Bone' Classic Rock
10	Family	Classic Jazz (Mingus, Monk, Parker, Coltrane, Petersen) Tom Petty
5	Family/self	Classic Reggae (Bob Marley) and Eason Chan
8	Self	Corridos Tumbados/Trap, LatinX Pop (Junior H), Reggaeton, [Female] HipHop
11	Family/self	Psychedelic /Inde Rock Pop, Synthpop (Tame Impala)
12	Self	New Wave; Post-punk (The Smiths, The Cure, Echo and The Bunnyman, Crowded House)
13	Family	80s and 90s Hip Hop (Tupac)
14	Family	Latin Jazz (Gabrielle Y Rodrigo) 'Lounge'/Classic Jazz (Monk, Coltrane, Mingus, Petersen)
17	Self	Classic Jazz (Mingus, Monk, Parker, Coltrane, Petersen) Ethiopian Music
7	Self	Santana
2	Family	Jesus Adrien Romero [Spanish] Christian Rock/Ballads
3	Family	Vivaldi Soundtrack to Forrest Gump BBC world news
15	Family/self	Classic Jazz (Brubeck, Monk, Davis, Petersen) Western classical (Mozart)
9	Family	Bay Area Hip Hop (Too$hort, E40, etc.) Earth Wind and Fire Miles Davis

Appendix 3.2: **Other Informants**

Mother of young man with coma after motor vehicle crash (MVC)

Mother of young man with coma after pedestrian versus automobile (PVA)

Partner of young man with traumatic brain injury (TBI) after bicycle crash

Sister of middle-aged man with coma after MVC and cerebral vascular accident (CVA)

Middle aged man with prolonged MV after blunt chest trauma

Bedside registered nurses

Sister of young woman with TBI after MVC

Medical doctors of neurology, critical care, surgery and neurosurgery: professors, and trainees

Wife and sister-in-law of man with TBI after crash

Middle aged woman after abdominal surgery

Middle aged man with tracheostomy and delirium after abdominal injury after assault

Resident doctors in training

Family of older woman after CVA

Advanced Practice Providers on the trauma service

Uncle and father of young man with penetrating trauma after gunshot assault

Parents and sister of young man with TBI and penetrating trauma after gunshot assault

Siblings of young man with gunshot assault

Appendix 3.3: **Focused Codes**

FOCUSED CODES	
Advocacy (Care/Respect) Alternate to medications Amnesia Anxiety Being Seen Boredom/Feeling Stuck Breathing Difficulties Calm/Becalming Cognition Coma Comfort/Soothe Communicating (when you can't speak) Community Confusion Connection Consciousness Control Coping/ inner strength Dancing (moving to music) Delirium Disconnected/De-situated Distraction Emotional pain Encouragement Enhanced focus Environment Familiar Family History Fear Focus Gratitude Happiness Healing Homelife Hope Humanizing Identity	Increasing communication Individuality Intrusive thoughts/PTSD Involving Family Joy Loneliness/Alone Making music Mechanistic/Dehumanized/Sterile Memories Mind Mindset Mood Music as a visitor Noise/Unpleasant sounds Normal Numbness/Resignation Pain Peace (Love/Pleasure) Positive thinking Presence Processing emotion (grief/loss) Psychological pain (relief) Relaxation Religion/ Spirituality Resilience Restraint Sadness Separation Silence Sleep Social Soul Stimulating senses Surviving/Doing Hard Things Unfamiliar Waking Up

Table 3.3: **Symptoms affected by music**

Loneliness Separation Fear Isolation Lack of sleep Anxiety Pain Grief Flashback Posttraumatic Stress Depression Sadness Dehumanization Intrusive thoughts Delirium Confusion De-situatedness Sensory deprivation Boredom Loss of control Dependence Numbness	Coping Belonging Happiness Joy Hope Resilience Connection Mood (Improved) Focus Pleasure Normalcy Self Determination Being Seen Identity

References

1. SCCM. http://www.sccm.org/Communications/Pages/CriticalCareStats.aspx 2018 [
2. Adhikari NK, Fowler RA, Bhagwanjee S, Rubenfeld GD. Critical care and the global burden of critical illness in adults. Lancet (London, England). 2010;376(9749):1339-46.
3. Granberg A, Bergbom Engberg I, Lundberg D. Patients' experience of being critically ill or severely injured and cared for in an intensive care unit in relation to the ICU syndrome. Part I. Intensive & critical care nursing. 1998;14(6):294-307.
4. Rotondi AJ, Chelluri L, Sirio C, Mendelsohn A, Schulz R, Belle S, et al. Patients' recollections of stressful experiences while receiving prolonged mechanical ventilation in an intensive care unit. Critical care medicine. 2002;30(4):746-52.
5. Lewandowska K, Mędrzycka-Dąbrowska W, Pilch D, Wach K, Fortunato A, Krupa S, et al. Sleep Deprivation from the Perspective of a Patient Hospitalized in the Intensive Care Unit-Qualitative Study. Healthcare (Basel). 2020;8(3):351.
6. Topcu S, Alpar S, Karabacak B, Kebapcı A. Patient experiences in intensive care units: a systematic review. Patient Experience Journal. 2017;4:115-27.
7. Von Rueden KT, Wallizer B, Thurman P, McQuillan K, Andrews T, Merenda J, et al. Delirium in Trauma Patients: Prevalence and Predictors. Crit Care Nurse. 2017;37(1):40-8.
8. Zaal IJ, Devlin JW, Peelen LM, Slooter AJ. A systematic review of risk factors for delirium in the ICU. Critical care medicine. 2015;43(1):40-7.
9. McGrane S, Pandharipande PP. Sedation in the intensive care unit. Minerva anestesiologica. 2012;78(3):369-80.

10. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. Anesthesiology. 2006;104(1):21-6.

11. Girard TD, Kress JP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. Lancet (London, England). 2008;371(9607):126-34.

12. Lat I, McMillian W, Taylor S, Janzen JM, Papadopoulos S, Korth L, et al. The impact of delirium on clinical outcomes in mechanically ventilated surgical and trauma patients. Critical care medicine. 2009;37(6):1898-905.

13. Pandharipande P, Cotton BA, Shintani A, Thompson J, Pun BT, Morris JA, Jr., et al. Prevalence and risk factors for development of delirium in surgical and trauma intensive care unit patients. The Journal of trauma. 2008;65(1):34-41.

14. Barr J, Fraser GL, Puntillo K, Ely EW, Gelinas C, Dasta JF, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Critical care medicine. 2013;41(1):263-306.

15. Burry LD, Williamson DR, Mehta S, Perreault MM, Mantas I, Mallick R, et al. Delirium and exposure to psychoactive medications in critically ill adults: A multi-centre observational study. Journal of critical care. 2017;42:268-74.

16. Ouimet S, Kavanagh BP, Gottfried SB, Skrobik Y. Incidence, risk factors and consequences of ICU delirium. Intensive care medicine. 2007;33(1):66-73.

17. Baumgarten M, Poulsen I. Patients' experiences of being mechanically ventilated in an ICU: a qualitative metasynthesis. Scandinavian journal of caring sciences. 2015;29(2):205-14.

18. Van Keer RL, Deschepper R, Huyghens L, Bilsen J. Mental well-being of patients from ethnic minority groups during critical care: a qualitative ethnographic study. BMJ open. 2017;7(9):e014075-e.

19. Puntillo K, Arai S, Cohen N, Gropper M, Neuhaus J, Paul S, et al. Symptoms experienced by intensive care unit patients at high risk of dying. Critical care medicine. 2010;38(11):2155-60.

20. Nikayin S, Rabiee A, Hashem MD, Huang M, Bienvenu OJ, Turnbull AE, et al. Anxiety Symptoms in Survivors of Critical Illness: A Systematic Review and Meta-Analysis. General hospital psychiatry. 2016;43:23-9.

21. Lof L, Berggren L, Ahlstrom G. ICU patients' recall of emotional reactions in the trajectory from falling critically ill to hospital discharge: follow-ups after 3 and 12 months. Intensive & critical care nursing. 2008;24(2):108-21.

22. Levitin D. This is your brain on music Canada Dutton Penguin; 2006.

23. Seashore C. Psychology of Music. New York: Dover Publications/McGraw-Hill Book Company; 1938/1967.

24. Farnsworth P. The Social Psychology of Music. 2nd ed. Ames, Iowa: The Iowa State University Press 1969. 298 p.

25. Zatorre RJ. Musical pleasure and reward: mechanisms and dysfunction. Annals of the New York Academy of Sciences. 2015;1337:202-11.

26. Sachs M, Habibi A, Damasio H. Reflections on music, affect, and sociality. Progress in brain research. 2018;237:153-72.

27. Damasio A. Descartes' Error. Emotion, Reason, and the Human Brain. New York: Grosset Putnam; 1994.

28. Habibi A, Damasio A. Music, feelings, and the human brain. US: Educational Publishing Foundation; 2014. p. 92-102.

29. Rorke MA. Music therapy in the age of enlightenment. J Music Ther. 2001;38(1):66-73.

30. Plato. The Collected Dialogues: Princeton University Press; 398 d-400a.

31. Gouk P. An Enlightenment proposal for music therapy: Richard Brocklesby on music, spirit, and the passions. Progress in brain research. 2015;217:159-85.

32. Tracy MF, Chlan L. Nonpharmacological Interventions to Manage Common Symptoms in Patients Receiving Mechanical Ventilation. Critical Care Nurse. 2011;31(3):19-29.

33. Tracy MF, Lindquist R, Savik K, Watanuki S, Sendelbach S, Kreitzer MJ, et al. Use of complementary and alternative therapies: a national survey of critical care nurses. Am J Crit Care. 2005;14(5):404-14; quiz 15-16.

34. Cooke M, Mitchell M, Tiralongo E, Murfield J. Complementary and alternative medicine and critical care nurses: a survey of knowledge and practices in Australia. Aust Crit Care. 2012;25(4):213-23.

35. Cutshall S, Derscheid D, Miers AG, Ruegg S, Schroeder BJ, Tucker S, et al. Knowledge, attitudes, and use of complementary and alternative therapies among clinical nurse specialists in an academic medical center. Clin Nurse Spec. 2010;24(3):125-31.

36. Meghani N, Tracy MF, Hadidi NN, Lindquist R. Part I: The Effects of Music for the Symptom Management of Anxiety, Pain, and Insomnia in Critically Ill Patients: An Integrative Review of Current Literature. Dimens Crit Care Nurs. 2017;36(4):234-43.

37. Puntillo K, Nelson JE, Weissman D, Curtis R, Weiss S, Frontera J, et al. Palliative care in the ICU: relief of pain, dyspnea, and thirst--a report from the IPAL-ICU Advisory Board. Intensive care medicine. 2014;40(2):235-48.

38. Marra A, Ely EW, Pandharipande PP, Patel MB. The ABCDEF Bundle in Critical Care. Critical care clinics. 2017;33(2):225-43.

39. Bradt J, Dileo C. Music interventions for mechanically ventilated patients. The Cochrane database of systematic reviews. 2014(12):Cd006902.

40. Richard-Lalonde M, Gélinas C, Boitor M, Gosselin E, Feeley N, Cossette S, et al. The Effect of Music on Pain in the Adult Intensive Care Unit: A Systematic Review of Randomized Controlled Trials. Journal of Pain and Symptom Management. 2020;59(6):1304-19.e6.

41. La G, Gerdner L. Evidence-Based Guideline: Individualized Music in Persons with Dementia (6th Edition). 2019.

42. Cardozo M. Harmonic sounds: complementary medicine for the critically ill. Br J Nurs. 2004;13(22):1321-4.

43. White JM. State of the science of music interventions. Critical care and perioperative practice. Crit Care Nurs Clin North Am. 2000;12(2):219-25.

44. Allen K, Golden LH, Izzo JL, Jr., Ching MI, Forrest A, Niles CR, et al. Normalization of hypertensive responses during ambulatory surgical stress by perioperative music. Psychosomatic medicine. 2001;63(3):487-92.

45. Heiderscheit A, Chlan L, Donley K. Instituting a music listening intervention for critically ill patients receiving mechanical ventilation: Exemplars from two patient cases. Music and medicine. 2011;3(4):239-46.

46. Fontaine DK. Nonpharmacologic management of patient distress during mechanical ventilation. Critical care clinics. 1994;10(4):695-708.

47. Heiderscheit A, Breckenridge SJ, Chlan LL, Savik K. Music preferences of mechanically ventilated patients participating in a randomized controlled trial. Music and medicine. 2014;6(2):29-38.

48. Chlan L. Effectiveness of a music therapy intervention on relaxation and anxiety for patients receiving ventilatory assistance. Heart & lung : the journal of critical care. 1998;27(3):169-76.

49. Chlan L, Engeland W, Anthony A, Guttormson J. Influence of music on the stress response in patients receiving mechanical ventilatory support: a pilot study. Am J Crit Care. 2007;16(2):141-5.

50. Chlan L, Weinert C, Heiderscheit A, Tracy M, Skaar D, Guttormson J, et al. Effects of patient-directed music intervention on anxiety and sedative exposure in critically ill patients receiving mechanical ventilatory support: a randomized clinical trial. Jama. 2013;309(22):2335-44.

51. Liang Z, Ren D, Choi J, Happ MB, Hravnak M, Hoffman LA. Music intervention during daily weaning trials—A 6-day prospective randomized crossover trial. Complementary therapies in medicine. 2016;29:72-7.

52. McCown W, Keiser R, Mulhearn S, Williamson D. The role of personality and gender in preference for exaggerated bass in music. Personality and Individual Differences. 1997;23(4):543-7.

53. Bonneville-Roussy A, Rentfrow PJ, Xu MK, Potter J. Music through the ages: Trends in musical engagement and preferences from adolescence through middle adulthood. Journal of personality and social psychology. 2013;105(4):703-17.

54. Alegria M, Canino G, Rios R, Vera M, Calderon J, Rusch D, et al. Inequalities in use of specialty mental health services among Latinos, African Americans, and non-Latino whites. Psychiatric services (Washington, DC). 2002;53(12):1547-55.

55. Roberts AL, Gilman SE, Breslau J, Breslau N, Koenen KC. Race/ethnic differences in exposure to traumatic events, development of post-traumatic stress disorder, and treatment-seeking for post-traumatic stress disorder in the United States. Psychological medicine. 2011;41(1):71-83.

56. Thorgaard K. Critique of influential epistemological presuppositions in clinical reasoning. European Journal for Person Centered Healthcare. 2013;1:124.

57. Charmaz K. Constructing Grounded Theory. 2nd ed: Sage Publications; 2014.

58. Nightingale F. Notes on Nursing. What It Is, And What It Is Not. Edinburg: Churchill Livingstone; 1859/1980.

59. Light KM. Florence Nightingale and holistic philosophy. J Holist Nurs. 1997;15(1):25-40.

60. Kakar E, Venema E, Jeekel J, Klimek M, van der Jagt M. Music intervention for sleep quality in critically ill and surgical patients: a meta-analysis. BMJ Open. 2021;11(5):e042510.

61. Qi W, Gevonden M, Shalev A. Prevention of Post-Traumatic Stress Disorder After Trauma: Current Evidence and Future Directions. Curr Psychiatry Rep. 2016;18(2):20-.

62. Maley JH, Brewster I, Mayoral I, Siruckova R, Adams S, McGraw KA, et al. Resilience in Survivors of Critical Illness in the Context of the Survivors' Experience and Recovery. Annals of the American Thoracic Society. 2016;13(8):1351-60.

63. Eghbali-Babadi M, Shokrollahi N, Mehrabi T. Effect of Family-Patient Communication on the Incidence of Delirium in Hospitalized Patients in Cardiovascular Surgery ICU. Iranian journal of nursing and midwifery research. 2017;22(4):327-31.

64. Wade DM, Hankins M, Smyth DA, Rhone EE, Mythen MG, Howell DCJ, et al. Detecting acute distress and risk of future psychological morbidity in critically ill patients: validation of the intensive care psychological assessment tool. Critical care (London, England). 2014;18(5):519-.

65. Petrowski K, Albani C, Zenger M, Brähler E, Schmalbach B. Revised Short Screening Version of the Profile of Mood States (POMS) From the German General Population. Frontiers in psychology. 2021;12.

66. Sun J, Chen W. Music therapy for coma patients: preliminary results. European review for medical and pharmacological sciences. 2015;19(7):1209-18.

67. Rahimi F, Saleh, K., Seidi, J. The effect of pleasant audio stimulation on the level of consciousness of comatose patient: a randomized clinical trial. Acta Medica Meditterranea 2019;35:985-9.

68. Yekefallah L, Namdar P, Azimian J, Dost Mohammadi S, Mafi M. The effects of musical stimulation on the level of consciousness among patients with head trauma hospitalized in intensive care units: A randomized control trial. Complementary therapies in clinical practice. 2021;42:101258.

69. Castro M, Tillmann B, Luauté J, Corneyllie A, Dailler F, André-Obadia N, et al. Boosting Cognition with Music in Patients with Disorders of Consciousness. Neurorehabilitation and neural repair. 2015;29(8):734-42.

70. Shors TJ, Anderson ML, Curlik DM, Nokia MS. Use it or lose it: How neurogenesis keeps the brain fit for learning. Behavioural Brain Research. 2012;227(2):450-8.

71. Canedo A, Grix MC, Nicoletti J. An analysis of assessment instruments for the minimally responsive patient (MRP): clinical observations. Brain injury. 2002;16(5):453-61.

72. Lombardi F, Taricco M, De Tanti A, Telaro E, Liberati A. Sensory stimulation for brain injured individuals in coma or vegetative state. The Cochrane database of systematic reviews. 2002;2002(2):CD001427-CD.

73. Magee WL, Clark I, Tamplin J, Bradt J. Music interventions for acquired brain injury. The Cochrane database of systematic reviews. 2017;1:Cd006787.

74. Siponkoski ST, Martínez-Molina N, Kuusela L, Laitinen S, Holma M, Ahlfors M, et al. Music Therapy Enhances Executive Functions and Prefrontal Structural Neuroplasticity after Traumatic Brain Injury: Evidence from a Randomized Controlled Trial. Journal of neurotrauma. 2020;37(4):618-34.

75. Elliott L, Walker L. Rehabilitation interventions for vegetative and minimally conscious patients. Neuropsychological Rehabilitation. 2005;15(3-4):480-93.

76. Stollings JL, Kotfis K, Chanques G, Pun BT, Pandharipande PP, Ely EW. Delirium in critical illness: clinical manifestations, outcomes, and management. Intensive care medicine. 2021;47(10):1089-103.

77. Oleson DS, Zubek JP. Effect of One Day of Sensory Deprivation on a Battery of Open-Ended Cognitive Tests. Perceptual and Motor Skills. 1970;31(3):919-23.

Chapter 4: Effect of A Recorded Music Listening Intervention on the Breathing Pattern of Mechanically Ventilated Adults

Abstract

Background: Critical illness and mechanical ventilation (MV) are associated with significant symptom burden including pain, anxiety, agitation, delirium, dyspnea and ventilator intolerance. Opioid and sedative medications, mainstays of symptom treatment in MV adults confer increased risk including prolonged length of MV and ICU stay and worsening delirium. In order to mitigate these risks, guideline-directed care of critically ill adults includes adjunctive non-pharmacological interventions for symptom management such as music-based interventions. Prior studies have demonstrated improved self-reported symptom experience associated with recorded music listening interventions (RMLI). However, there remains a lack of reliable objective measure of the effects of RMLI in MV adults. This pilot study examines the effect of an RMLI on ventilator derived breathing measures as a proxy for autonomic nervous system relaxation.

Methods: A convenience sample of MV adults receiving volume control (VCV) or pressure support ventilation (PSV) were observed during exposure to a 45-minute RMLI using self- or family-selected playlists in this quasi-experimental repeated measures, pretest-posttest design study. Continuous breath-by-breath data was extracted using a Philips NM3® respiratory profile monitor including respiratory rate (RR) (breaths/min), breath-by-breath time interval (sec); expired tidal volume V_T (L); minute ventilation V_E (L/min); peak inspiratory airway pressure (PIP); peak inspiratory and expiratory flowrates (PIF, PEF); and rapid shallow breathing index (RSBI).

Results: 16 MV adults completed 22 RMLI observation periods. There were no significant pre-post differences in any of the breathing outcome measures after a single 45-minute RMLI. Median RR, V_T, V_E, PEF, PIP, MAP, and number of extra breaths were unchanged in the VCV group (n=12) after an RMLI. In the PSV group (n=10) median RR, V_T, V_E, PIF, PEF, RSBI breath-breath interval were also the same before during and after an RMLI. Music selections varied widely across the group.

Conclusions: RMLIs are acceptable interventions for symptom management for MV adults in critical care. Future studies that explore clinical outcomes of breathing, such as time to extubation, success of extubation, tolerance of weaning modes, or dyspnea score, among others, are recommended.

Key Words: Music Based Intervention, Mechanical Ventilation, Breathing, Symptom, Relaxation

Background

Critical illness and mechanical ventilation (MV) are associated with significant symptom burden including pain, anxiety, agitation, delirium, immobility, and sleep disturbances (PADIS) (1-5). In addition, patients who receive MV also complain of air hunger, gagging, choking and being *out of sync* with the ventilator (6). Opioid and sedative medications, the mainstay of treatment for the symptoms of PADIS, are used to promote tolerance of MV. However, both confer increased risk of delirium and morbidities such as prolonged length of MV and ICU stay (7, 8). Conversely, undertreated symptoms of PADIS and ventilator intolerance are also associated with medium- and long-term morbidity such as the development of chronic pain syndrome and post-traumatic stress disorder (9, 10). Guideline-directed care of critically ill adults includes adjunctive non-pharmacological treatments for PADIS such as music-based interventions (MBIs) as a means to mitigate the morbidity associated with pharmacologic symptom management in MV (11).

MBIs are used across health care settings to promote psychological and physical health (12). MBIs may be delivered in critical care units in several ways including: as live music, played by musicians; as an intervention delivered by trained and licensed music therapists (music therapy); or as recorded music listening interventions (RMLIs) delivered by clinicians (music medicine) (13). Listening to recorded music has been associated with reductions in subjective reports of pain, anxiety, and general discomfort among MV adults (14, 15). However, randomized controlled trials of RMLIs for symptom management in MV adults unable to self-report have failed to demonstrate consistent benefit. The lack of convincing findings may be related to the measurements used to establish effect. Commonly selected physiological measurements such as mean heart rate, blood pressure, and respiratory rate (RR) are poorly

correlated with PADIS, states of agitation and sedation experienced by MV patients (16). Psychometric instruments designed to measure agitation and sedation such as the Richmond Agitation Sedation Scale (RASS) or observed pain such as the Critical Care Pain Observation Tool (CPOT), lack specificity for people experiencing ventilator intolerance because they include any observation of ventilator intolerance in their construct for agitation, even if otherwise unresponsive (17, 18).

The autonomic nervous system (ANS) is largely responsible for the involuntary regulation of physiologic and psychologic stability (19). There is emerging evidence to support an association between physiological correlates of the ANS and some emotional states such as anxiety, fear and pleasure or joy (20, 21). The ANS processes signals from the body and the mind leading to alterations in the balance of parasympathetic and sympathetic systems activation which affect physical and emotional response (22). Listening to music may have effects on the ANS via the limbic and hypothalamic-pituitary axis resulting in physical signs and psychological reports of relaxation, anxiolysis, and emotional reward (23-25). Therefore, measures of the ANS may serve as reliable instruments to gauge response to stimuli (either noxious or pleasant) within an individual (21, 26). This mechanism is thought to be activated by an emotional response to music, based on memories of music and cognitive processing of musical stimuli (27, 28).

ANS activation also stimulates central respiratory drive, balancing both random and nonrandom influences to achieve gas exchange homeostasis (29). This manifests as excitatory changes in the breathing pattern. Specifically, this includes increased RR, depth of breathing (i.e. tidal volume, V_T), inspiratory muscle pressure and inspiratory flow demand, and thus is a psychophysiological expression of emotion (21). Noxious stimulation of the ANS correlates to increased respiratory drive, which may manifest as increased RR and pulmonary pressures (30).

Mean RR is among the most commonly studied respiratory measurement of ANS response to music interventions (19). However, intermittent measures of mean RR are not consistently affected by music interventions in MV (31-46). One reason for this lack of findings is the inclusion of patients treated with controlled breathing modes that include a fixed minimum mechanical breath rate, thereby limiting potential variance due to basement effect. Studies of RMLI in MV patients conducted during ventilator weaning, a spontaneous mode of ventilation without a set mechanical rate, suggest that music interventions may be associated with decreased RR (39, 47, 48). Further, RR may not be a sensitive marker for changes in autonomic balance as *respiratory drive* must increase by at least 3 times the resting value before there is a commensurate change in overall RR (49). A more discrete measure of ANS stimulation is likely required to detect response to RMLI in highly confounded populations such as are found in critical care.

Other neurally mediated measures of breathing depth such as V_T or surrogates of inspiratory muscle pressure reflect respiratory drive and may be more sensitive to physical or psychological stimulus (49). Breathing *pattern* may also vary with psychological and physical states or in response to external stimulus such as music. Common measures of breathing patterns or effort include: minute ventilation (V_E); rapid shallow breathing index (RSBI); and peak inspiratory flow (Appendix 2 and 3). Small changes in depth and pattern of respiration have been measured as V_T, V_E, and RSBI alongside a RMLI in two studies (39, 48). Though small, these studies are some of the first to include ventilator measures which may correlate to RMLIs. No studies of MV adults receiving fixed rate MV examine changes in the occurrence of patient-initiated breaths or peak inspiratory pressure (PIP).

There remains a lack of a reliable, objective measure of the effects of RMLI in MV adults. We suggest that changes in breathing mediated by stimulation of the ANS are a theoretically grounded measure of response to a music stimulus. Therefore, the purpose of this exploratory pilot study is to examine the effect of a preferred, recorded, music listening intervention on 1) Breathing rate, depth (PIP and MAP), and pattern during volume control ventilation, and 2) Breathing rate (RR), depth (V_T) and pattern (PIF, RSBI, $V_{E,}$) among MV adults during spontaneous breathing mode.

Methods

Study Sample and Design

A quasi-experimental, repeated measures, pretest-posttest design was employed. All participants were observed before, during, and after a RMLI during volume control and pressure support ventilation, with a recruitment goal of 20 participants. Institutional Review Board approval was obtained from the Committee for Human Research at the University of California, San Francisco.

Participants and Setting

A convenience sample of participants was recruited from the Surgical and Neuroscience ICUs (SICU/NSICU) in a single, level one trauma center in San Francisco, California, from August 2020 to November 2021. Inclusion criteria were age 18 years old or greater, undergoing MV after traumatic injury or emergency surgery, on stable ventilator settings of either volume control or pressure support ventilation, stable sedation regimens and predicted to need MV for more than 24 hours. Exclusion criteria were known, severe hearing loss (as reported by family members or noted in the medical records), severe agitation (RASS >+2), deep sedation (RASS < -3), psychotic disorder or evidence of psychosis, psychiatric hold, pregnancy, hemodynamic

instability (ongoing resuscitation during hemorrhage, active up-titration of vasoactive infusions, tachycardia >130 beats/min, unstable cardiac rhythm), chemical paralysis, use of continuous dialysis, severe or worsening hypoxia (FiO2 80%, up-titration of FiO2 within the past 6 hours), forensic custody, isolation for infection, or not deemed suitable by the primary treating team (e.g., anticipated transition to comfort care). Potential participants were identified by bedside clinicians who had been briefed on the study aims and were screened for inclusion by a single member of the research team (RM). If suitable for inclusion, participants or their legally authorized representatives were approached for consent. Proxy consent to obtain physiological measurements was obtained from patients' legally authorized representatives. If participants regained the ability to communicate during hospitalization, they were informed of the study and reconsented. Analysis was stratified by mode of ventilation into two groups: volume control and pressure support.

Music Intervention

Once consented, a member of the research team (RM) worked with participants, their family, and friends to select approximately 45 minutes of music for the RMLI. Music was selected through several means. Some families chose specific music (albums, particular songs) and identified these to the PI through email or by phone. Most families made broad suggestions of music based on genre, era, or artist. Next, the PI used a web-based application to search for specific music requests (songs or albums) or by artist or genre based on family and patient preference. Families (and interactive patients) then reviewed any playlists generated by the web-based application and approved or amended the selections. Playlist requirements were that music must be included while recordings of nature sounds, spoken word (audiobooks, talk radio) were excluded. No restrictions to tempo, beat, rhythm, instrument, genre, timbre, or mood were placed

on music selections. Playlists were then loaded into a web-based music application on a study-tablet. Music was delivered through tablet speakers and placed on a stand near the head of the bed in each patient's room during the intervention period. Speaker volume was increased until responsive patients endorsed hearing music through gestural assent (nodding, thumbs up).

Procedure

All participants were observed between 7 AM and midnight. Each observation period was at least 75 minutes long and started with a baseline 15-minute observation interval, followed by a 45-minute music listening intervention interval, and at least a 15-minute post music observation interval. Prior to initiation of observations, participants were placed in a semi-recumbent position, all care was clustered, and interruptions were minimized to only those necessary for patient safety and comfort such as suctioning, pain relief, attendance to alarms and patients in distress. All such interruptions were noted on the data collection sheet.

Measurements

Baseline clinical characteristics during each observation period were recorded by a member of the research team (RM) including RASS, CPOT, Glasgow Coma Score (GCS), Confusion Assessment Method (CAM) score for delirium screening, as well as infusion rates for all sedatives, opioids, and psychoactive medications. Administration of all additional sedative or analgesic medications during the study period was documented on a data collection tool. Ventilator settings (volume control or pressure support), level of positive end expiratory pressure (PEEP), and fraction of inspired oxygen (FiO2) were recorded for all observations. During volume control ventilation, machine-delivered set respiratory rate and tidal volume V_T (ml) were documented on the data collection sheet. During pressure support ventilation, machine-delivered pressure above PEEP was recorded on the data collection tool. Other clinical and demographic

characteristics were extracted from the electronic health record and through interviews with patients and families.

Breathing variables were measured using an NM3® (Philips, Carlsbad, CA) noninvasive pulmonary mechanics monitor which underwent standard calibration procedures by staff respiratory therapists prior to being connected to ventilator circuits and which remained in place throughout the study period. Flash drives were placed into the NM3® devices to record breath data, downloaded to a laptop, and processed with breath-by-breath data using software provided by Philips.

Extracted data points and their dimensions included the RR (breaths/min), breath-by-breath time interval (sec), expired V_T (L), expired V_E (L/min) peak inspiratory airway pressure (PIP) in cmH_2O, peak inspiratory and expiratory flowrates (PIF, PEF) expressed in L/min, and RSBI expressed as breaths/min/L. For participants receiving volume control ventilation, number of spontaneous breathing efforts were calculated by subtracting the number of machine-delivered breaths from the total measured RR ('extra' breaths/min).

Outcome Measures

Breath rate was operationalized as RR for each mode of ventilation (pressure support and volume control) and 'extra-breaths' for the volume control group. Depth of breathing was operationalized as V_T (mL) for both modes of ventilation. PIP and MAP (cm H20) were examined as indirect measures of chest wall compliance and surrogate measures of depth in the volume control group. Respiratory pattern was operationalized as V_E (L/min) for both modes of ventilation, as RSBI and breath- breath interval (sec) for the pressure support group, and as PIF for the volume control group. Continuous data were analyzed and grouped into mean values

within 5-minute increments starting 10 minutes before the intervention and for at least 60 minutes after the intervention was initiated.

Statistical Analysis

Comparison of participant demographic and clinical variables between both modes of ventilation was conducted with Student's t-test and Pearson's Chi-squared test using STATA 16. Extracted ventilator data were analyzed using R v4.1.0 (50). Any physiologically out of range value was discarded (i.e., PIP >70 mmHg). We analyzed 7 outcomes for both modes of ventilation: RR, VT ,VE, PIF, PEF for all conditions, PIP and MAP for those receiving volume control, and breath by breath time interval (seconds) and RSBI for those receiving pressure support. Time courses were initially plotted for each outcome and were visually examined for any difference in outcomes from interruptions noted during observation (such as suctioning or administration of extra pain medication). We windsorized the values of each individual (lower and upper 5%) for better data visualization. Windsorizing is a data transformation technique wherein the influence of extreme values are minimized by folding a portion of the highest and lowest values into the data set (51). We further binned the outcome in 5-minute intervals (with the exception of the last measurement in 'music on' had a larger bin size as not everyone was followed on music for exactly the same time, although they were generally similar), and calculated the median value in the bin (to be more robust to outlier values than the mean). Finally, we fit a mixed effects linear regression model for the binned outcome measurements with the R package lme4 v1.1.27.1 (52) and tested for differences in time periods compared to the first baseline 5-minute interval. The alpha level was set at 0.05.

Results

Thirty potential participants were identified through census review or recommendation from clinical staff. One person declined to participate, citing concerns over music being 'too activating' for his family member. Of the remaining 29, all expressed interest in study participation. Six potential participants were unable to enroll due to changing clinical conditions resulting in either extubation or clinical instability identified in the exclusion criteria. Three consented participants were extubated prior to enrollment, one died unexpectedly, and three others were unable to complete any measurement due to administrative issues (Figure 4.1).

Sixteen participants completed 22 intervention and observations periods (PSV only=4, VCV only=6, both=6). Social and demographic characteristics were equivalent across both groups. All but two of the participants was male (n=14) with a mean age of 38.31 (13.01) (Table 4.1). Two participants identified as professional musicians, and 2 more identified as avocational musicians (played instruments or sang as a pastime in their communities). Ventilator settings used during music interventions were volume control ventilation (n=12) and pressure support ventilation (n=10) (Table 4.2). Participants observed during volume control ventilation were enrolled on hospital day 7 (3.49), ventilator day 7 (3.54) whereas observations during pressure support mode were on hospital day 12 (9.35) and ventilator day 10 (8.05). Eleven study participants had traumatic brain injury (TBI) and 9 had thoracic injuries. Fourteen participants had endotracheal airways and 2 had tracheostomies in place. At the time of enrollment all but one participant was confused (CAM positive) or too obtunded to be assessed for confusion. Mean GCS (8.83 vs 8.8, p=0.97, moderately depressed consciousness) and RASS (-2 vs -1.8, p=0.72, light sedation) were the same at the start of the intervention in both groups. During volume control ventilation 11 (91.7%) participants were receiving continuous sedation infusions

(propofol and/or dexmedetomidine) and 9 (75.0%) were receiving continuous opioid infusions (fentanyl or hydromorphone). Continuous sedation and opioid infusions were used in 6 (60%) participants during pressure support ventilation.

Music selections were made by family members (n=12), patients (n=3), and in one case, clinician suggestion (n=1) when no family were able to provide a music recommendation. Playlist contents are presented in appendix 4. Music selections were played for 41-60 minutes in 13 of the observations. Several participants indicated they wanted to continue listening to the music after the planned intervention; in these cases, the music was left on for up to 20 more minutes in 6 cases and indefinitely in 3 cases. Interventions occurred in the afternoon (n=13), morning (n=2) or at night (n=1).

There was no significant difference in any of the measured breathing outcomes after music intervention. In the pressure support ventilation group mean RR, V_T ,V_E, PIF, PEF, RSBI breath-breath interval were also the same before during and after a music intervention (Figures 4.2-4.8). Mean RR, V_T,V_E, PEF, PIP, MAP, and number of extra breaths were unchanged in the volume control group after music intervention (Figures 4.9-4.15).

Discussion

This is the first study to test the effect of a music intervention on continuous, respiratory and ventilator-derived data. As an exploratory study, our primary interest was to learn about the feasibility of continuous respiratory measurements as an outcome measure for music intervention studies. Data acquisition and extraction from the NM3® devices was straightforward and generated high quality continuous objective measurements. While this novel study did not yield statistically significant changes over time in these measures, methodological insights gained can

be used to inform future trials designed to measure the effects of music interventions on measures of breathing in MV patients.

Length of Intervention

Unlike prior studies that demonstrated a change in RR, V_T, and RSBI, (39, 48) we did not document a difference in these measurements before and after a music listening intervention in the group receiving pressure support ventilation. There are several possible explanations for this outcome. One reason may be related to the length of our music intervention. We examined the use of a 45-minute (or longer) music intervention, whereas others have utilized shorter RMLI. Jaber et al noted an increase in V_T and a decrease in RR and RSBI after only 10 minutes in their cross over design study of 15 people during ventilator weaning (39). However, these differences were not maintained after 15 minutes of music; by the end of the intervention, both V_T and RSBI had returned to baseline. Synn and Choe reported similar findings of reduction in RR, RSBI and an increase in V_T after a brief (30 minute) intervention with relaxing classical music in 21 adults (48). This group also observed a similar rapid onset of effect and rapid return to baseline afterwards, with all participants returning to baseline within the 30-minute washout period. These immediate effects have been noted in other studies of music interventions. For example, a recent meta-analyses in critical care patients using music interventions for treatment of pain found significant improvement only after music interventions lasting between 20 and 30 minutes, but not after interventions of less than 20 minutes or greater than 30 minutes (14). Others have shown reduction in procedural pain (such as with suctioning, turning, or bathing), with short music interventions (40, 53, 54).

Advances in cognitive neuroscience have enriched understandings of the mechanism of action of music listening in the brain. Current frameworks point to an activation of the pleasure

and reward system involving the limbic, hypothalamic pathways and to cognitive processing in the auditory cortex and prefrontal cortices (23, 25, 55, 56). While research indicates that processing music involves multiple cognitive processes, including attention (57), it is not known how long a critically ill person in a highly stimulating environment can maintain attention on a music stimulus. It is possible that our observation and intervention periods were too long, and that the short-lasting effects of listening to music faded or were overwhelmed by other confounds in a busy ICU in participants with possible impaired attention.

Clinical Heterogeneity of Subjects

A more likely explanation lies in the clinical heterogeneity of the study participants, in particular their altered mental states. Eleven (68%) study participants had TBI. Brain injury is known to alter breathing patterns directly though injury to the lungs and also indirectly due to autonomic nervous system dysfunction (58). Prior research of breathing patterns suggests that changes in respirations are common among people with TBI (59). Opioid and sedative use in this cohort may also have affected the results. Most studies of music interventions for MV ventilated adults exclude people who are deeply or continuously sedated. However, there is evidence to suggest that people can hear and are positively affected by music delivered while under anesthesia (60-63). Despite the high doses of sedating medications and overall low level of consciousness in our group, we were able to verify with all but one patient that they could hear the music. Nevertheless, breathing responsiveness during periods of altered mental status remains unclear. Opioids and benzodiazepines may cause respiratory depression through reduction in RR and tidal volume (64). Propofol lowers the central nervous system response to oxygenation and ventilation (65) but ketamine may *stimulate* respiratory centers resulting in

increased respirations (66-68). It is likely that any measurable effect from an RLMI was confounded by high doses of sedatives and opioids administered in our small sample.

All but one of the participants in our study screened positive on the CAM test indicating a high likelihood of delirium. The defining features of delirium are cognitive relating to perception or awareness, and the subtypes are often differentiated by motor response as hyperactive, hypoactive, or mixed (69). Individuals with delirium may be agitated or somnolent, but all have a decrease in executive function; some endorse hallucination; others experience confusion (70). It is well established that MV is associated with increased risk of delirium, but the effects of delirium on MV are not known. In other words, it is not clear what effect a hyperactive state may have had on the measured breathing indices. Examination of the distribution plots reveals significant difference in the total variance between individuals, suggesting an important difference in arousal level at baseline. Further, delirium may affect an individual's response to music interventions. Research has shown that stroke patients demonstrate improved awareness, attention span, and mood after listening to 'pleasant music' (57), pointing to a possible use for the treatment of delirium. Though promising, new music interventions designed to prevent or treat delirium have not yet shown a benefit (71).

Heterogeneity of Music Selections

Music selection heterogeneity may also have influenced our results. Current recommendations for RMLIs in critical care emphasize patient preference and familiarity (72-76). Both Liang and Jaber offered participants a choice of music genre, but both also limited the selections to music considered 'relaxing', based on slow tempo. Similarly, Synn and Choe tested slow tempo Western classical music against traditional Korean music noting a greater response to Korean music in their trial of 21 people during ventilator weaning (48). One large prospective

trial of MBIs in MV adults in North America (n=107) identified classical, jazz, rock, country and 'oldies' (1950-1970) as the most commonly preferred genres of music (77). However, the generalizability of these recommendations is threatened by the lack of participant diversity; all but one participant identified as white, with a mean age of 60 years. Research suggests music preference may depend on sex, age, social determinants such as income, education level and place of origin, and music background (24). While mostly male, our study participants were younger and more diverse in terms of racial and ethnic identity, socio-economic status, place of origin, and musical background. These differences were reflected in the wide variety of music chosen by family members and also by the 2 participants who made their own selections. Several participants or their surrogates chose slow tempo 'relaxing' music (Enya, classical, religious, jazz), but some selected faster, more upbeat music of varying genres including reggaeton, hip hop, Latin jazz, and post punk alternative rock.

Many researchers advocate for the use of slow tempo music (60-80 beats/min) in critical care (73, 74, 78). However, in people with TBI, preferred music of any tempo has been associated with greater reduction in agitation than 'relaxing' slow temp classical (79). Others have shown equal reduction in RASS between both patient-selected preferred music and investigator-selected 'relaxing classical' music in MV adults (80). We cannot know what contribution music selection made to the study outcome given the small sample size, and propose that future studies explore the variety of personally selected music used in RMLIs in diverse populations.

Use of Objective Continuous Data

Finally, the validity of studies reporting a difference in RR, V_T, and RSBI may be threatened by observer bias, whereas our results were based on an objective measure. Prior

studies that examined breathing after RMLIs were based on clinicians' observations of a small sample of breaths recorded at specific intervals during the study period. It is possible that if these prior analyses included a comprehensive, machine sourced survey of all of the breaths during the study periods, then observed differences may have been moderated. Conversely, our rich continuous data was vulnerable to confounds such as coughing, mucous plugging, or kinks in the ventilator tubing, events that trained observers would dismiss during their observations. We attempted to account for these unusual or external circumstances during the data cleaning process, though several outliers remained unaccounted for leaving open the possibility of other instrument-related measurement errors.

Limitations

This study has several limitations. First, there was a high rate of attrition as 30% of consented participants were unable to complete an intervention and observation session, and of 16 enrolled participants only 6 completed both sessions of music interventions. The most common reason for this was worsening or improving clinical condition. Enrollment was further hampered by clinical care requirements including operations, diagnostic imaging, consultant team rounds, rehabilitation therapy, blood draws and dressing changes. Identifying a 2-hour period of relative clinical stability without interruption in such a complex population in a NSICU/SICU proved unfeasible. However, the high symptom burden of injured, surgical patients enjoins us to design studies that include this vulnerable population. Limiting the length of future interventions to 30 minutes of music and examining the period of time during ventilator weaning may help attend to these enrollment problems.

Small sample size may also threaten the validity of our findings. As an exploratory pilot study of a novel measurement, our main objective was to investigate the use of breathing indices

as a measure of response to an RLMI. As such, we were able to demonstrate wide acceptability of a personalized music intervention with over 95% of potential participants expressing interest in enrollment. We are encouraged by the interest of patients and their family members who overwhelmingly agreed, or requested, to listen to music. Information gained from this pilot can shape future studies of RMLI in critical care.

Finally, the sensitivity and specificity of the outcome measures we explored are not well established for change in arousal, or relief of unpleasant symptoms; it is likely that they also lack sensitivity for RMLIs. For example, the administration of sedatives and analgesia have proven ineffective at reducing ventilator intolerance. More specifically, sedatives and analgesia have failed to moderate breath stacking or early, extra breathing, leading some to recommend changes to the *ventilator* rather than treatment of the *patient* (81). Also, V_E has demonstrated sensitivity to noxious stimuli in people under general anesthesia, but it is not known what effect a pleasant stimulus may have on breathing patterns (82). Importantly, subtle changes in breathing measures after RMLIs identified in previous studies lack clinical significance. Liang et al showed that listening to preferred music was associated with an improved tolerance for ventilator weaning, as measured by reduction in dyspnea and increased spontaneous breathing mode time length (47). Studies like these that include clinically meaningful outcomes help explain the relationship between RMLIs, breathing and symptom experience.

Conclusion

Measurements of breathing did not change after a personalized RMLI in this small pilot study of sedated, MV adults. The amount of variance differed greatly between individuals and may reflect important differences in arousal level between individuals, which likely confounded our results. Widespread enthusiasm among participants and family members for the use of

RMLIs suggests that listening to music is of some subjective benefit. Studies that restrict enrollment to a more heterogenous sample of patients who are awake and calm or lightly sedated, may help uncover a consistent change in breathing indices associated with RMLIs. Future studies that explore clinical outcomes of breathing such as time to extubation, success of extubation, tolerance of weaning modes, or dyspnea score, among others are recommended.

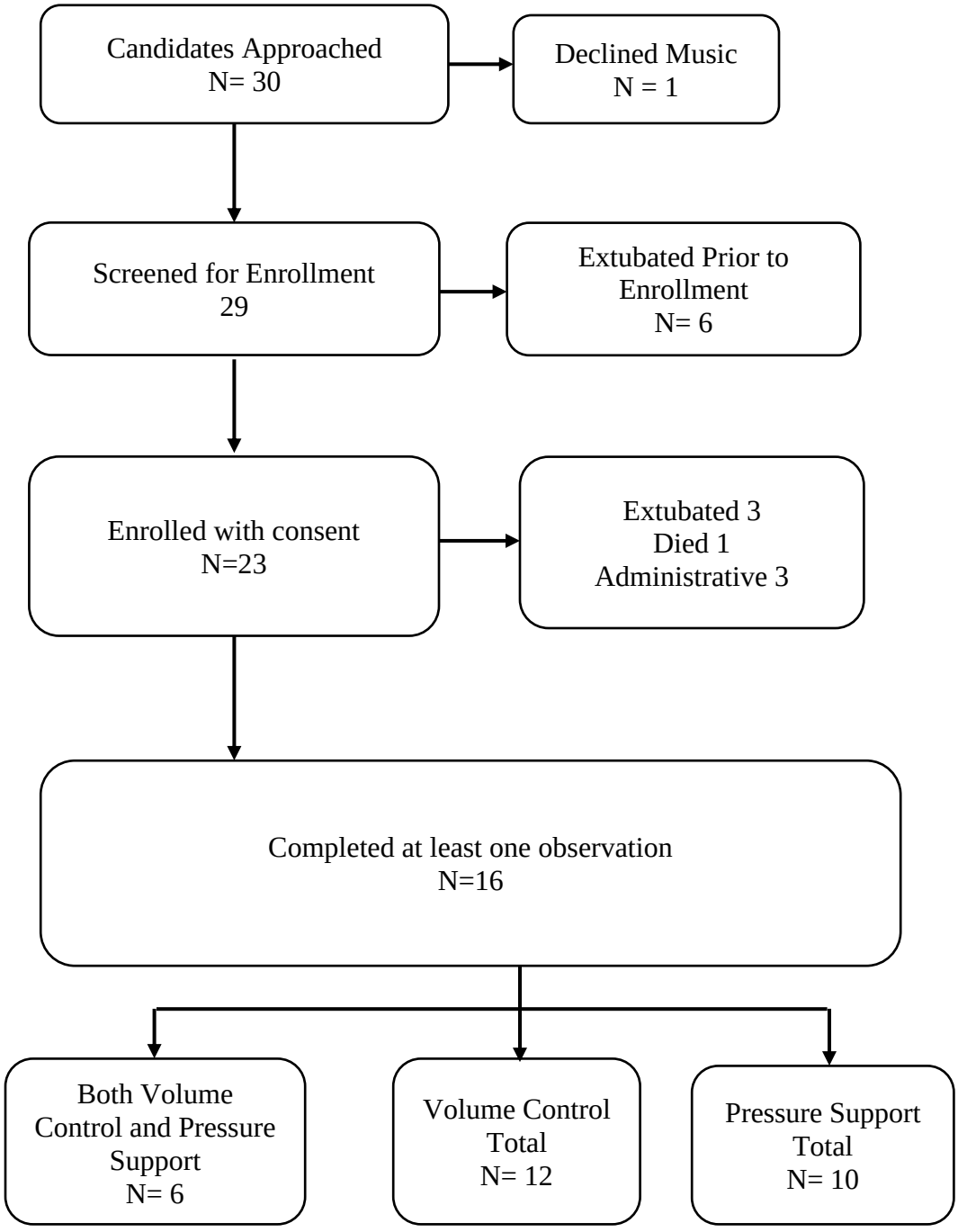


Figure 4.1: **CONSORT Flow Diagram**

Table 4.1: **Sample Characteristics**

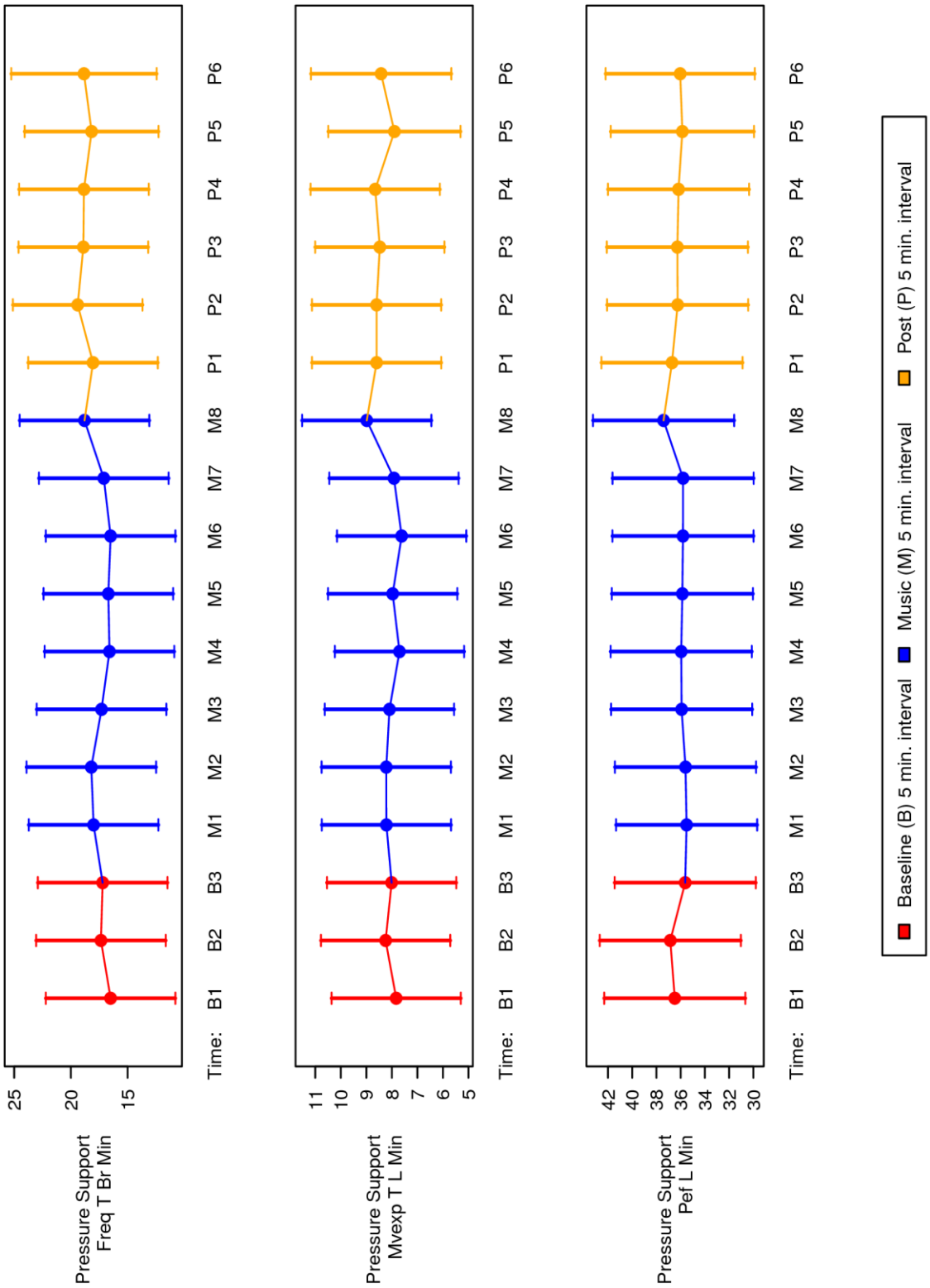
Characteristics, N (%) or mean (SD)	**N=16**
Age: Mean years, (range, SD)	38.31, (25-64, 13.01)
Sex: female male non-binary	 2 (12.5%) 14 (87.5%) 0 (0%)
Race or Ethnicity: Asian Black/African American LatinX Native American White Decline	 4 (25.5%) 2 (12.5%) 1 (6.2%) 1 (6.2%) 7 (43.8%) 1 (6.2%)
Primary Language Spoken: English Spanish Cantonese	 12 (87.5%) 1 (6.2%) 1 (6.2%)
Religion: Buddhist Christian/Catholic Muslim None	 1(6.2%) 2 (12.5%) 1 (6.2%) 12 (75%)
Insurance: Private MediCal	 8 (50.0%) 8 (50%)
Housing: Housed Unhoused Unstable housing	 11(68.8%) 4 (25%) 1 (6.2%)
Employment: Employed Unemployed	 8 (50%) 8 (50%)

Table 4.2: **Baseline Characteristics**

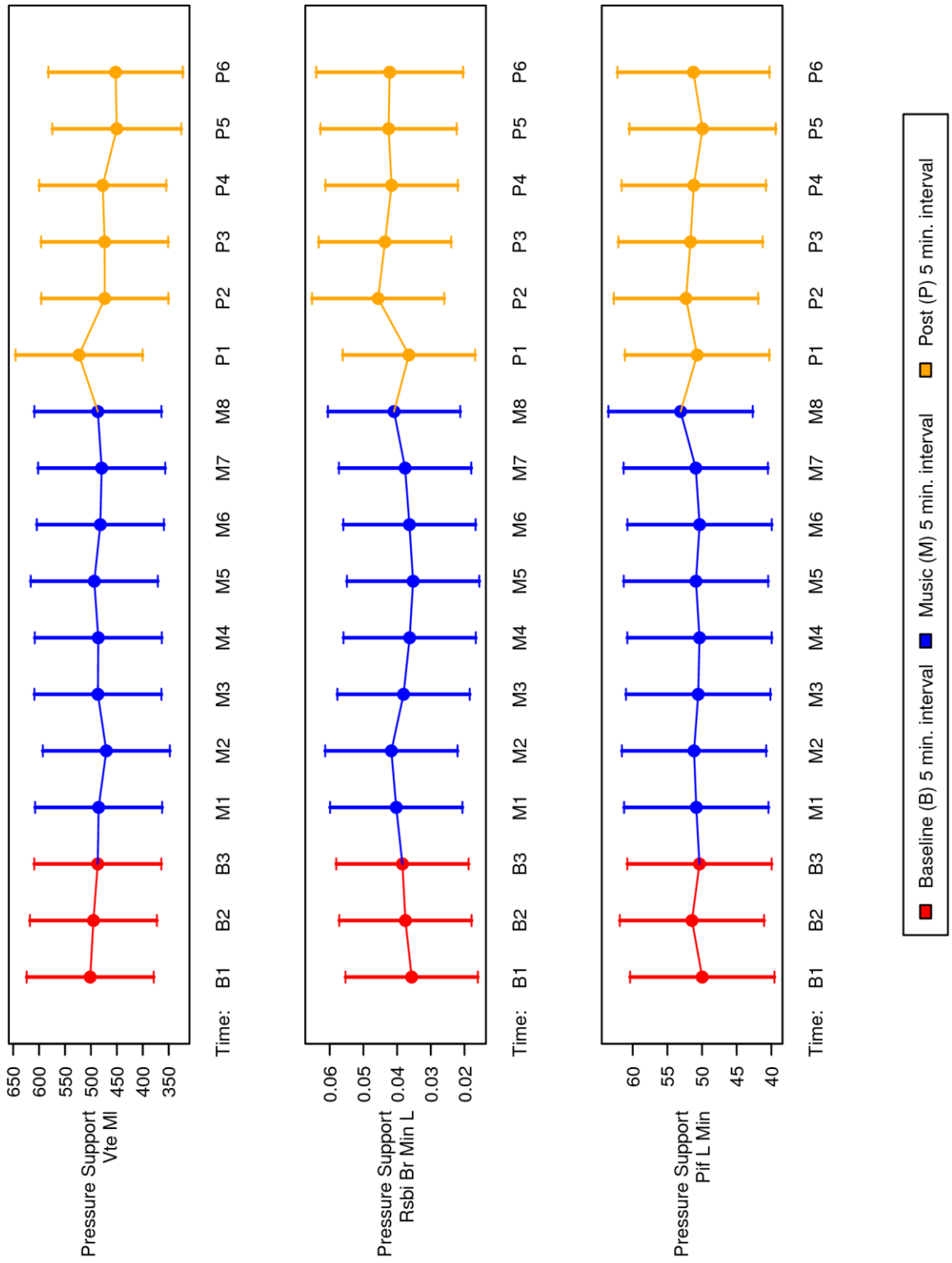
Clinical Characteristics	**Volume control [N= 12]**	**Pressure Support [N= 10]**	**P value**
Hospital Day: mean (SD)	7.17 (3.49)	12.40 (9.35)	0.087[1]
Ventilator Day: mean	7.00 (3.54)	9.80 (8.05)	0.289[1]
Presence of TBI yes (%)	8 (66.7%)	7 (70.0%)	0.867[2]
Thoracic trauma: yes (%)	6 (50.0%)	7 (70.0%)	0.342[2]
CAM* + yes (%) no (%) unable to assess	10 (83%) 1 (8.3%) 1 (8.3%)	8 (80%) 0 (0%) 2 (20%)	0.381[2]
RASS*: mean (SD)	-2.00 (1.35)	-1.8 (1.23)	0.722[1]
GCS*: mean	8.83 (2.41)	8.80 (1.55)	0.970[1]
Continuous Infusion yes (%) Sedative Opioid	 11 (91.7%) 9 (75.0%)	 6 (60.0%) 6 (60.0%)	 0.078[2] 0.452[2]
Propofol mcg/kg/min mean (SD)	38.57 (25.45)	31.67 (14.38)	0.569[1]
Fentanyl mcg/hr. mean (SD)	160.71 (116.24)	162.50 (103.08)	0.403[1]
Precedex mcg/min mean (SD)	1.03 (0.40)	1.27 (0.46)	0.403[1]
Ventilator Characteristics			
Airway ETT* Tracheostomy	 1 (8.3%) 11 (91.7%)	 3 (30%) 7 (70%)	 0.190[2]
FiO2*: mean (SD)	42.50 (8.66)	40.50 (8.64)	0.595[1]
PEEP*: mean (SD)	7.92 (1.98)	7.20 (2.04)	0.414[1]
Tidal Volume ml mean (SD)	548.33 (105.56)	NA	NA
Respiratory Rate	13.73 (2.41)	NA	NA
Pressure support above PEEP	NA	7.80 (1.75)	NA

1. Linear Model ANOVA
2. Pearson's Chi-squared test

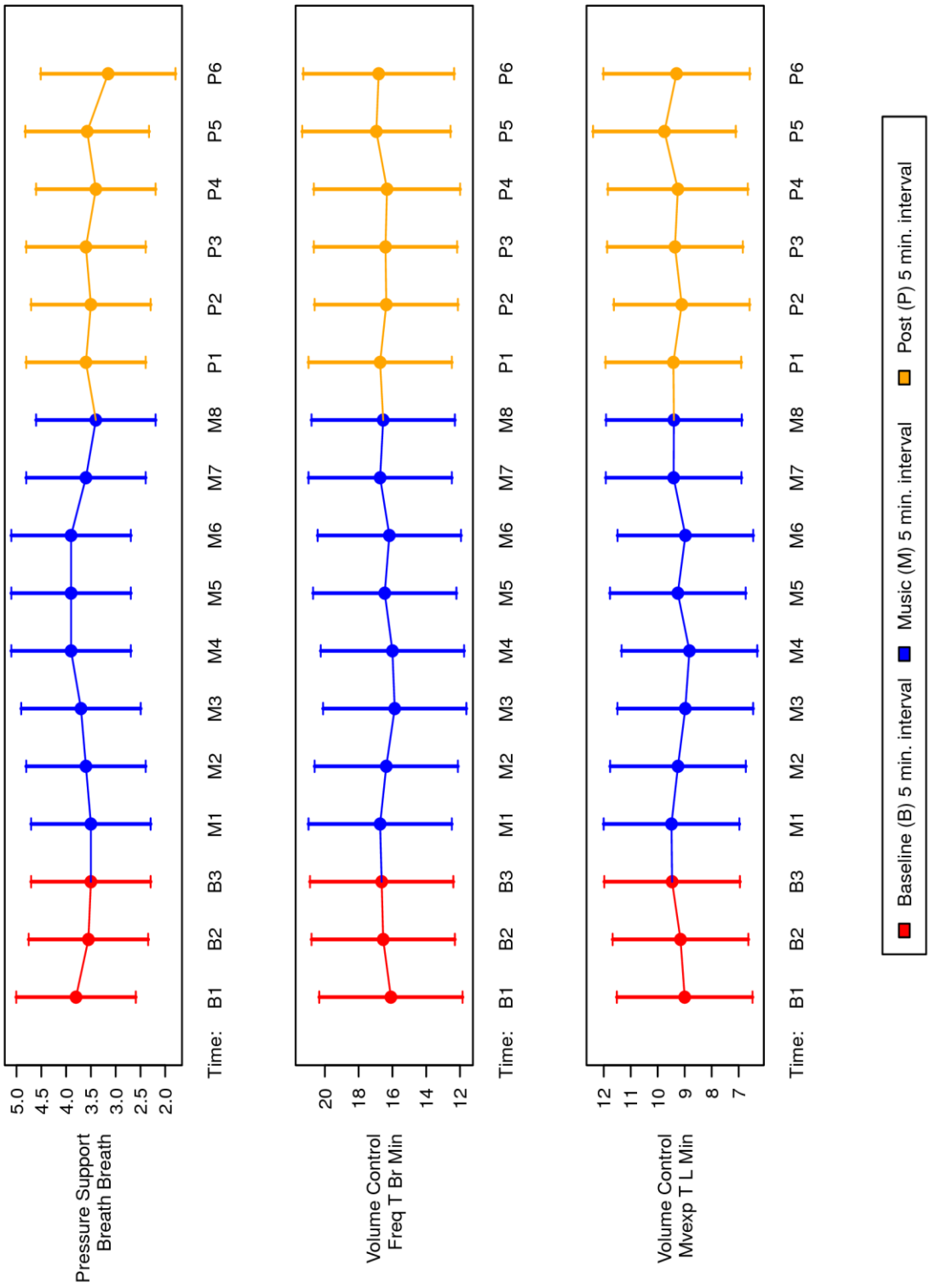
Key of abbreviations: CAM: Confusion Assessment Method; RASS: Richmond Agitation Sedation Score; GCS: Glasgow Coma Score, mcg: micrograms; min: minute; kg: kilograms; hr.: hour; ETT: Endotracheal Tube; TBI: traumatic brain injury; FiO2: Fractional inspired Oxygen, PEEP: positive end expiratory pressure; mcg: microgram; SD: standard deviation



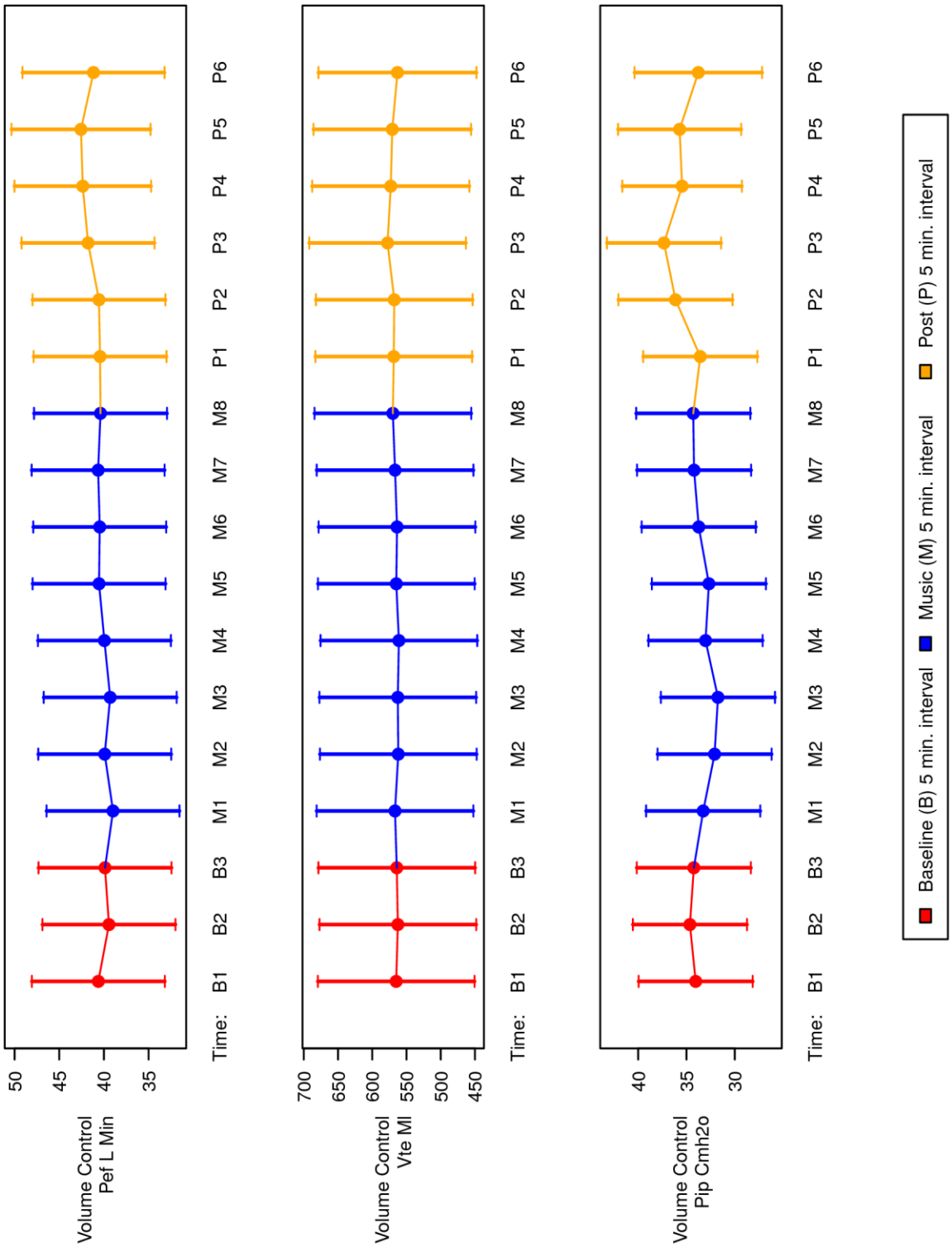
Figures 4.2-4.4: Pressure Support Breathing Measure Outcomes: Respiratory Rate, Minute Ventilation, and Peak Expiratory Flow



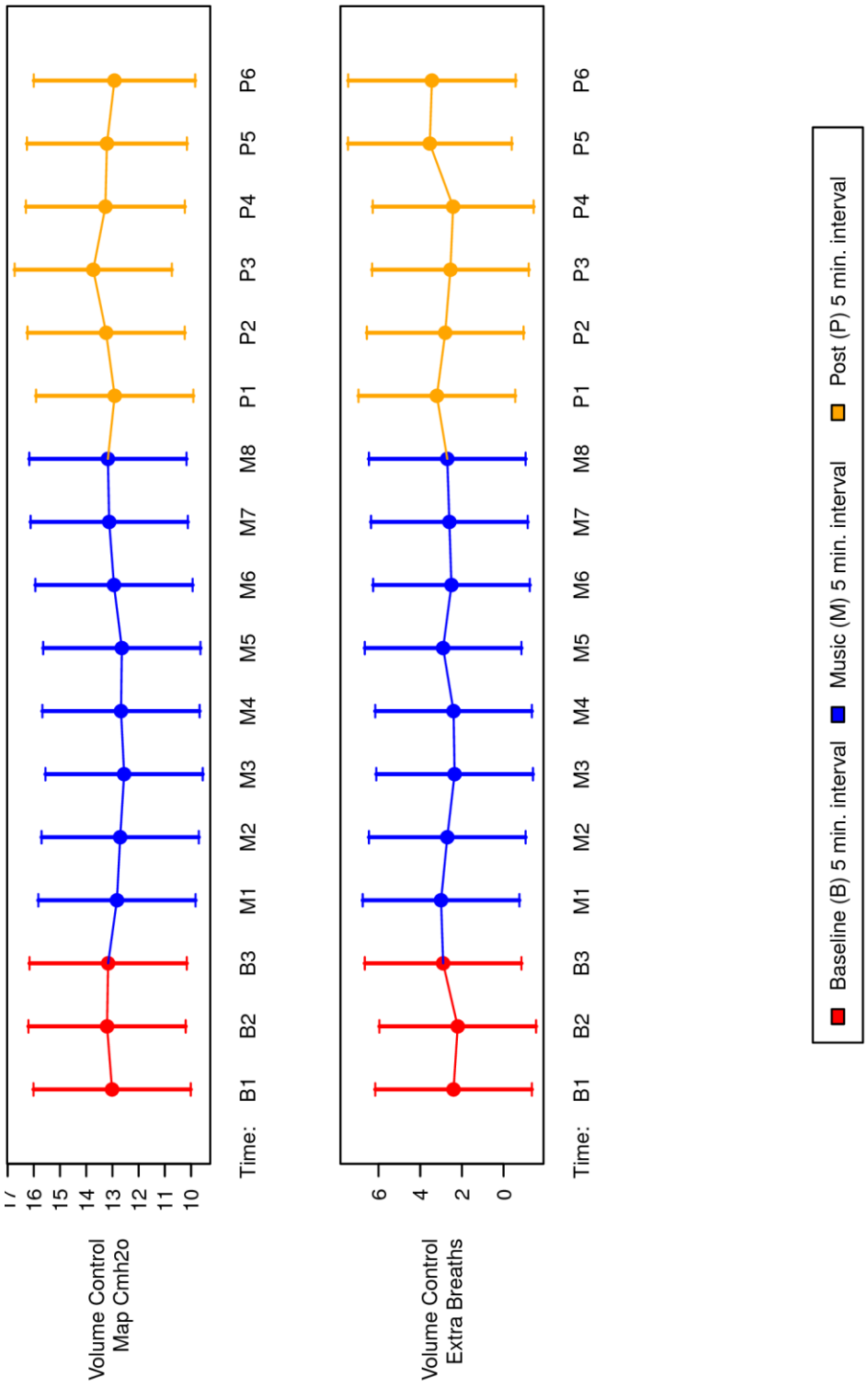
Figures 4.5-4.7: Pressure Support Breathing Measure Outcomes: Tidal Volume, Rapid Shallow Breathing Index, Peak Inspiratory Flow



Figures 4.8-4.10: Pressure Support Breathing Measure Outcome: Breath-Breath interval; Volume Control Breathing Measure Outcome: Respiratory Rate, Minute Ventilation



Figures 4.11-4.13: Volume Control Breathing Measure Outcomes: Peak Expiratory Flow, Tidal Volume, Peak Inspiratory Pressure



Figures 4.14-4.15: Volume Control Breathing Measure Outcomes: Mean Airway Pressure, Extra Breaths.

Appendix 4.1: **Abbreviations**

Concept	Abbreviation	Description
Richmond Agitation Sedation Scale	RASS	10-point Likert scale of agitation and sedation centered on 0 = awake and calm (-5 comatose - +4 combative)
Critical Care Pain Observation Scale	CPOT	12-point psychometric scale of observed pain for use in critical care
Glasgow Coma Scale	GCS	15-point psychometric scale (3-15) of level of consciousness
Confusion Assessment for ICU Score	CAM-ICU	Dichotomous (+ or -) screen for delirium in critical care
Pain, Anxiety/Agitation, Delirium, Immobility and Sleep	PADIS	Constellation of symptoms targeted by the Society of Critical Care Medicine for management for improved outcomes

Appendix 4.2: **Breathing Measures**

Breathing Measure	Definition	Abbreviation
Volume Control Ventilation	Machine delivers fixed rate of breaths of a specific volume per minute	VCV
Pressure Support Ventilation	Patient initiates all breaths, once triggered, machine delivers breath according to preset driving pressure which determines inspiratory flow (L/min)	PSV
Fraction of inspired oxygen	Concentration of oxygen in gas mixture (%)	FiO2
Respiratory Rate	Number of breaths per minute	RR
Breath-Breath interval	Time between initiation of each breath (seconds)	Breath-Breath interval
Tidal Volume	Volume in Liters of breath delivered	V_T
Tidal Volume expired	Volume in Liters of breath on expiration	
Positive end expiratory pressure	Minimum pressure preserved in the circuit at the end of a breath cycle (cm H20)	PEEP
Peak inspiratory airway pressure	Highest pressure measured in the breath cycle; represents both resistance and compliance (cm H20)	PIP
Peak Inspiratory flowrate	L/min	PIF
Peak Expiratory flowrate	L/min	PEF
Rapid Shallow Breathing Index	Ratio of number of breaths/min to the tidal volume in L of breaths	RSBI

Appendix 4.3: **Explanation and justification of Breathing Measures**

V_E is the product of V_T and RR and normally reflects metabolic demand, but it also reflects supra-pontine input from the limbic, paralimbic and sensory/motor cortices associated with panic, anxiety, and pain (29, 83). RSBI is RR/V_T (84) and elevated RSBI > 100 is associated with the inability or difficulty to sustain unassisted breathing (85). Classically excessive work of breathing in pulmonary disease worsens dyspnea and frequently induces anxiety (86, 87). Therefore, monitoring RSBI possesses at least face validity as a potential surrogate for assessing the work of breathing associated with critical illness. Inspiratory flow and V_T reflect change in the muscular contraction of the chest during spontaneous breathing; as respiratory drive increases so too does the velocity of muscular contraction and thus flow rate (88). As such, peak inspiratory flow may reflect change in respiratory drive, signaling a change in the somatic state after an RMLI. Peak inspiratory pressure (PIP) represents the total force generated by the mechanical ventilator to overcome resistance in the lungs, airways and the chest wall (89). Thus, increased tension of the chest wall muscles in response to noxious stimulus or increased respiratory drive may be reflected as increased PIP measured by the mechanical ventilator during volume-controlled ventilation (88).

Appendix 4.4: **Music Selections**

Participant 2: both sessions
Artist chosen by girlfriend, endorsed by uncle, later validated by patient
45 minutes
Dame Este Monte, Jesus Adrian Romero, Daniel Santoy (Coleccion Duetos) 3:40; Algo Mas, Jesus Adrian Romero (El Brillo De Mis Ojos) 4:41; Jesus, Jesus Adrian Romero, Marcos Vidal (Coleccion Duetos) 3:48; Tu Estas Aqui, Jesus Adrian Romero, Marcela Gandara (Coleccion Duetos) 4:57; Mi Universo, Jesus Adrian Romero (El Aire De Tu Casa) 4:13; Sumegerme, Jesus Adrian Romero (Coleccion Adoracion) 5:28; Estas Aqui, Benjamin Rivera (Dias Mejores) 4:52; Mi Entorno, Jesus Adrian Romero (Ayer Te Vi….Fue Mas Claro Que La Luna) 4:04; La Ultima Palabra, Daniel Calveti (Vivo para Ti) 4:24; Me Dice Que Me Ama, Jesus Adrian Romero (El Aire De Tu Casa) 4:02; El Padre Que Siempre Sone, Abel Zavala (Listo Para Nuestro Encuentro) 3:24

Participant 3
Composition chosen by wife and daughter
51 minutes
Vivaldi, The Four Seasons, Violin Concerto in E Major Op 8, No 1, RV 269 "Spring" I. Allegro; Giuliano Carmignola, Sontari de la Giosa Marca 3:12; Vivaldi, The Four Seasons, Violin Concerto in E Major Op 8, No 1, RV 269 "Spring" II. Largo e pianissmo sempre, Giuliano Carmignola, Sontari de la Giosa Marca 2:16; Vivaldi, The Four Seasons, Violin Concerto in E Major Op 8, No 1, RV 269 "Spring" III. Danza pastorale, Giuliano Carmignola, Sontari de la Giosa Marca 3:41; Vivaldi, The Four Seasons, Violin Concerto in G Minor Op 8, No 2, RV 315 "Summer" I. Allegro non molto, Giuliano Carmignola, Sontari de la Giosa Marca 5:03; Vivaldi, The Four Seasons, Violin Concerto in G Minor Op 8, No 2, RV 315 "Summer" II. Adagio presto, Giuliano Carmignola, Sontari de la Giosa Marca 2:13; Vivaldi, The Four Seasons, Violin Concerto in G Minor Op 8, No 2, RV 315 "Summer" III. Presto, Giuliano Carmignola, Sontari de la Giosa Marca 2:22; Vivaldi, The Four Seasons, Violin Concerto in F Major Op 8, No 3, RV 293 "Autumn" I. Allegro, Giuliano Carmignola, Sontari de la Giosa Marca 4:46; Vivaldi, The Four Seasons, Violin Concerto in F Major Op 8, No 3, RV 293 "Autumn" II. Adagio, Giuliano Carmignola, Sontari de la Giosa Marca 2:36; Vivaldi, The Four Seasons, Violin Concerto in F Major Op 8, No 3, RV 293 "Autumn" I. Allegro, Giuliano Carmignola, Sontari de la Giosa Marca 2:53; Vivaldi, The Four Seasons, Violin Concerto in F Minor Op 8, No 3, RV 297 "Winter" I. Allegro non molto, Giuliano Carmignola, Sontari de la Giosa Marca 3:07; Vivaldi, The Four Seasons, Violin Concerto in F Minor Op 8, No 3, RV 297 "Winter" II. Largo, Giuliano Carmignola, Sontari de la Giosa Marca 1:49; Vivaldi, The Four Seasons, Violin Concerto in F Minor Op 8, No 3, RV 297 "Winter" III. Allegro, Giuliano Carmignola, Sontari de la Giosa Marca 2:47

Participant 5: both sessions
Playlist determined by Spotify (popular Easan Chan); artist suggested by partner
69 and 70 minutes
Artist Eason Chan: 不期而遇的夏天 Unexpected Summer 3:30；世界上不存在的歌 A Song That Doesn't Exist in the World 3:53；孤勇者 Lone Brave 4:16; 十年 Decade 3:25; 我們 We

4:20; 因為愛情 Because of Love 3:36; 淘汰 Eliminate 4:45; 好久不見 Long Time no See 3:26; 明年今日 Next Year Today 4:10; 單車 Bike 3:31; 富士山下 Under Mt Fuji 4:19; K歌之王 King of K Songs 3:38

Participant 9:
Music picked by bedside nurse and respiratory therapist, confirmed by sisters
60 minutes
It's Lit Playlist (on Spotify); first and second session ; 93 'Til infinity by Souls of Mischief (93 Til Infinity): 4:46; Blow The Whistle* by Too $hort (Blow the Whistle): 2:43; Super Hyphe (Original*) by Keak Da Sneak (Keak Da Sneak's Greatest Hits): 3:34; Choices Yup by Golden State Warriors Remix- E40 (Choices Yup Golden State Warriors Remix): 2:42; 4am Bay Bridge Music* by Andre Nickatina and Equipto (Gun Mouth 4 Hire, Horns and Halos #2): 3:39; San Francisco Anthem feat. Big Rich and Bod Banga by San Quinn, Big Rich, Bod Banga (Rydah J Klide Slap House Vol 2) 4:57; R.I.P.* by Jeezy, 2 Chainz (R.I.P.) 3:20This D by TeeFLii, Mustard (This D) 3:05; Like Waaat feat. Bad Lucc* by Problem (Understand Me-EP) 3:32; Versace Remix* by Migos, Drake Versace (Versace Remix Drake single) 4:06; Kung Fu by Baauer, Pusha T, Future (Kung Fu): 2:40; 4 Lit* by B.o.B. T.I. Ty Dolla $ign (4 Lit): 3:24; Gas Pedal* by Sage the Gemini, Iamsu! (Gas Pedal): 3:27 ; Feek-A-Leek* by Petey Pablo (Still Writing in My Diary: 2nd Entry): 3:55; Wicked *by Future (EVOL): 2:53Jump* feat. Gizzle by Lupe Fiasco, Gizzle (DROGAS Light): 4:35; Hit the Gas* feat. Snoop Dogg & Nef the Pharoah by Raven Felix, Snoop Dog, Nef the Pharoah (Hit the Gas Snoop Dog, Nef the Pharoah) 3:36; Slappin* by E-40, Nef the Pharoah, Shelley FKA DRAM (Slappin) 3:50; Moves* by Big Sean (I Decided.) 3:50Come Get Her* by Rae Sremmurd (SremmLife) 3:33

Participant 10:
Music selected by mother, later confirmed by patient
45 minutes
Jazz Classics on Spotify: Blue in Green (feat. John Coltrane & Bill Evans), Miles Davis, John Coltrane and Bill Evans (Kind of Blue Legacy Edition), 5:38; Goodbye Pork Pie Hat, Charles Mingus (Ah Um) 5:42; Stormy Weather, Oscar Peterson Trio (Plays the Harold Song Book) 3:33; A Day in the Life: by Wes Montgomery (Wes Montgomery: Finest Hour) 5:49; In a Sentimental Mood, by Duke Ellington, John Coltrane (Duke Ellington & John Coltrane) 4:15; Blue in Green (feat. John Coltrane & Bill Evans), Miles Davis, John Coltrane and Bill Evans (Kind of Blue Legacy Edition), 5:38; A Love Supreme, Pt 1, John Coltrane (A Love Supreme) 7:43; Footprints, Wayne Shorter (The Best of Wayne Shorter) 7:32 Bumpin' On Sunset, Wes Montgomery 4:49; 'Round Midnight, Thelonious Monk (Genius of Modern Music) 3:41; It Might as Well Be Spring, Bill Evans Trio (Moon Beams) 6:06; So What (feat. John Coltrane & Bill Evans), Miles Davis, John Coltrane and Bill Evans (Kind of Blue Legacy Edition 9:22

Participant 11:
Music selection by mother and sister
60 minutes
Artist: Bad Bunny (patient later changed to Tame Impala)
Lo Siento BB: (with Bad Bunnny & Julieta Venegas) 3:27; Yonaguni* 3:26; X Ultima Vaz* 3:12; X Utlima Vez* 3:12; Volvi* 3:50; MIA (feat. Drake) 3:30; LA CANCION, feat J Balvin

(Oasis) 4:02; A Tu Merced 2:55; La Santa* 3:26; La Cancion 4:02; Volando*- Remix 4:33; La Zona* 2:16, Vete* (YHLQMDLG) 3:12; Desde El Corazon 2:07; Si Veo a Tu Mama 2:51; La Dificil* 2:43; Te Mudaste* 2:10; Otra Noche en Miami* 3:53; Diles (feat Arcangel, Nengo Flow, Dj Luian & Mambo King) 4:39; Yo Perreo Sola 2:52;

Participant 12:
Self-selected by patient, with changes and song by song selection (sometimes interrupted) took controls into their own hands
66 minutes
The Smiths, Morrisey, The Cure, Velvet Underground, Joy Division, The English Beat, Echo and the Bunnymen, Elvis Costello, Squeeze, REM

Participant 13:
Music chosen by siblings, confirmed during and later with patient
63 minutes
Genre: 90s Hip Hop on Spotify; Hypnotize, The Notorious B.I.G. (Life After Death) 3:50; No Diggity*, Blackstreet, Dr Dre, Queen Pen (Another Level) 5:05; Ambitions As a Ridah, 2 Pac (All Eyez on Me) 3:50; Rosa Parks*, Outkast (Aquemini) 5:24; I Wish, Skee-Lo (I wish) 4:09; Shoop Salt-N-Pepa (The Best of Salt-N-Pepa) 4:07; California Love- Original Version, 2 Pac, Roger, Dr Dre (The Best of 2Pac) 4:44; Push-It Salt-N-Pepa (The Best of Salt-N-Pepa) 4:29; Hip Hop Hooray*, Naughty by Nature (booty Phat Classics) 4:25; It Was A Good Day*, Ice Cube (The Predator) 4:20; C.R.E.A.M. Wu-Tang Clan, Method Man, Raekwon, Ispectah Deck (Enter the Wu-Tang) 4:12; Killing Me Softly With His Song, Fugees, Ms Lauren Hill (The Score) 4:59Runnin'* The Pharcyde (Labcaincalifornia) 4:56

Participant 14:
Chosen by partner, in the moment assented by patient (later listened to Jazz classics, preferred it though had declined it in the moment)
66 minutes
Artist: Rodrigo Y Gabriela
Oblivion (the Jazz EP) 5:13; Vikingman- Remastered 4:02; Hanuman 3:43; Street Fighter Mas (The Jazz EP) 5:47; South of Heaven's Chanting Mermaids- From Pirates of the Caribbean 5:46; Stairway to Heaven 4:44; Orion 7:44; 30 De Marzo 4:14; Tamacun 3:25; Angry and Dead Again- From Pirates of the Caribbean 3:53; Lingus 8:39; Senorita XXX 4:24

Participant 15:
Chosen by parents and sibling, assented by patient once conscious:
Session 1: 60 minutes
Miles Davis: Kind of Blue followed by other selections of Davis
Kind of Blue: So What (feat John Coltrane, Cannonball Adderley & Bill Evans) 9:22; Freddie Freeloader (feat John Coltrane, Cannonball Adderley, Wynton Kelly, Paul Chambers) 9:46; Blue in Green (feat John Coltrane & Bill Evans) 5:37; All Blues (feat John Coltrane, Cannonball Adderley & Bill Evans) 11:37; Flamenco Sketches (feat John Coltrane, Cannonball Adderley & Bill Evans) 9:26; Generique (The Columbia Years 1955-1985) 2:46; It Never Entered My Mind, (Jazz Inspiration) 4:04; Drad Dog (The Original Mono Recordings) 4:32

Session 2:
88 minutes
John Coltrane
A Love Supreme: Part I Acknowledgment (A Love Supreme) 7:43; In a Sentimental Mood, Duke Ellington and John Coltrane (Duke Ellington & John Coltrane) 4:15; and John Coltrane My One and Only Love John Coltrane and Johnny Hartman 4:54; Too Young To Go Steady, John Coltrane Quartet (Ballads) 4:21; How Deep is The Ocean, John Coltrane, Hal Mobley. Al Cohen, Zut Sims (Interplay Box Set) 15:06; After the Rain, John Coltrane (Impressions) 4:09; A Love Supreme: Part IV Psalm 7:02; Say It (Over and Over Again), John Coltrane Quartet (Ballads) 4:15; You Don't Know What Love Is, John Coltrane Quartet (Ballads) 5:12; IT's Eady To Remember, John Coltrane Quartet (Ballads) 2:45

Participant 16: both sessions
Music selected by son, some of the artists personally known to them
56 and 61 minutes
Cantonese Worship music on Spotify: 天地讚美 Heaven and earth praise 3:42; 祢是王 You are the King 3:53; 我心尊主為大 My heart is great for the Lord 3:00; 誰曾應許 Who ever promised; 愛是不保留 4:02; Love is not reserved 4:02; 耶和華是愛 Jehovah is love 4:56 ; 全因為祢（劉美娟）All because of You (Liu Meijuan) 4:31; 我信愛是恆久 I believe that love is eterna 4:32l; 全因為你（鄧婉玲）All because of you (Tang Wanling) 4:42; 當你走到無力時 When you come to powerlessness 4:14; 一首讚的詩歌 A poem of praise 4:16

Participant 18:
Artist chosen by mother and sister, later endorsed as a favorite by patient
70 min
Artist: Bob Marley: Three Little Birds (Exodus), 3:00; Could You Be Loved (Uprising) 3:57; Is This Love (Kaya) 3:52; Jammin (Legend) 3:31; One Love (Exodus) 2:53; Buffalo Soldier (Confrontation) 4:16; Redemption Songs (Uprising) 3:54; Waiting in Vain (Legend) 4:16; No Woman No Cry 7:08; Satisfy my Soul (Kaya) 4:31; Rebel Music 6:45; Burnin' and Lootin' (Burnin') 4:13

Participant 19:
Selected by spouse, endorsed by patient, then patient took over the controls and changed it after 30 minutes to a pre-selected 'sleep music' on own device.
No end
Initially: Enya album Shepherd Moons: Shepherd Moon 3:46 Caribbean Blue by Enya (Shepherd Moons) 4:00 How Can I Keep from Singing? 4:26 Ebudae 1:56Angeles 4:01No Holly for Miss Quinn 2:56 Book of Days 2:56 Evacuee 3:51Lothlorien 2:07 Marble Halls 3:56

Participant 20 session 1:
Suggested by clinical staff after R+B mix seemed to make them anxious
69 min

The Most Relaxing Classical Ever, a playlist on Spotify: Canon in D Johann Pachelbel, Orchestre de Chambre, Jean-Francois Paillard 6:16 Eine kleine Nachtmusick: Andante Wolfgang Amadeus Mozart, Camereta Academica, Franceso Macci 5:52Fur Elise Ludwig van Beethoven, Sylvia Capova 2:50 Strong Quartet No 1 Pyotr Illyicj Tchaikovsky, Shostakovich Quartet 6:42Clare De Lune Claude Debussy, Latvian Philharmonic Chamber Orchestra, Illmar Lapinsch 4:21Idyl for Strings: Adagio Loes Janacek, Prague chamber Orchestra 5:41Adagio in G Minor, Tomaso Albinoni, Ilmar Lapinsch, Latvian Philharmonic Orchestra 8:31The Girl with Flaxen Hair Claude Debussy, Jacques Rouvier 2:17Air on a G String, Johann Sebastian Bach, Royal Philharmonic Orchestra, Frank Shipway 3:25Greensleeves, Ralph Vaughn Williams, Philharmonic Orchestra 4:33 Largo from Xerxes, George Frideric Handel, Maxence Larrieau, Susanna Mildonian 4:11Prelude in C, Johann Sebastian Bach, Valrey Afanassiev 1:57The Planets: Venus Gustave Holst Royal Philharmonic Orchestra 8:05Goldberg Variations: Aria Johann Sebastian Bach, Konstantin Lifschitz 2:11Adagio For Strings Samuel Barber, I Solisti Italiani 7:01

Participant 20 session 2
Reggaeton Mix
58 min
Selected by nurses who had cared for patient in prior hospitalizations, daughter assented to choice: Guasam Guasa* by Tego Calderon (El Abayarde) 4:00; Aventura by Luny Tunes, Noriega, Wisin & Yandel (Mas Flow, Vol 1) 2:51; La Calle Me Lo Pidio, by Yandel, Tego Calderon (Quien Contra Mi) 3:06; Ven Pegate, by Arcangel (De La Ghetto, Zion) 3:55; Hasta el Amanecer, by Nicky Jam (Fenix) 3:19; Aqui Esta Tu Caldo, by Daddy Yankee (Blin Blin, Vol 1) 3:32; El Mellao, by Volto (En Lo Claro) 3:43; Villana, by Hector & Tito (Blin Blin, Vol 1) 2:24; Cuano Baila Reggaeton, by Tego Calderon, Yandel (The Underdog- El Subestimado) 3:04; Vamos Pa' La Disco, by Las Guanabanas (Guillaera) 2:48

Participant 21 session 1
Selected by parents
50 min
Eagles: Take It Easy 3:31; Witchy Woman 4:10; Lyin' Eyes 6:21; Already Gone 4:15; Desperado 3:33; One of These Nights 4:51; Tequila Sunrise 2:53; Take it to the Limit 4:45; Peaceful Easy Feeling 4:17; The Best of My Love 4:34; Hotel California 6:31

Participant 21 Session 2
Selected by Parents
41 min
"Easy Rock" (aka Yacht Rock): Faithfully, Journey (Frontiers) 4:27; Don't Stop Believin', Journey (Escape) 4:11; Open Arms, Journey (Escape) 3:22; I Want to Know What Love Is, Foreigner (Agent Provocateur) 5:05; Waiting For A Girl Like You, Foreigner (4 Expanded) 4:52; Alone, Heart (Bad Animals) 3:39; Take it on the Run, REO Speedwagon (Hi Infidelity) 4:00; Every Rose Has Its Thorn, Poison (Open Up and Say Ahhh!) 4:20; Sister Christian, Night Ranger (Midnight Madness) 5:03; Come Sail Away, Styx (The Grand Illusion) 6:07; Who's Crying Now, Journey (Escape) 5:00; Hotel California, Eagles (Hotel California) 6:31; Juke Box

Hero, Foreigner (4 Expanded) 4:20; Feel Like Makin' Love- 2015 Remastered, Bad Company (Straight Shooter) 5:14

Participant 22
Music selected by wife and sister-in-law
60 min
"Easy Rock" (aka Yacht Rock): Faithfully, Journey (Frontiers) 4:27; Don't Stop Believin', Journey (Escape) 4:11; Open Arms, Journey (Escape) 3:22; I Want to Know What Love Is, Foreigner (Agent Provocateur) 5:05; Waiting For A Girl Like You, Foreigner (4 Expanded) 4:52; Alone, Heart (Bad Animals) 3:39; Take it on the Run, REO Speedwagon (Hi Infidelity) 4:00; Every Rose Has Its Thorn, Poison (Open Up and Say Ahhh!) 4:20; Sister Christian, Night Ranger (Midnight Madness) 5:03; Come Sail Away, Styx (The Grand Illusion) 6:07; Who's Crying Now, Journey (Escape) 5:00; Hotel California, Eagles (Hotel California) 6:31; Juke Box Hero, Foreigner (4 Expanded) 4:20; Feel Like Makin' Love- 2015 Remastered, Bad Company (Straight Shooter) 5:14
*Explicit Lyrics

References

1. Granberg A, Bergbom Engberg I, Lundberg D. Patients' experience of being critically ill or severely injured and cared for in an intensive care unit in relation to the ICU syndrome. Part I. Intensive & critical care nursing. 1998;14(6):294-307.
2. Rotondi AJ, Chelluri L, Sirio C, Mendelsohn A, Schulz R, Belle S, et al. Patients' recollections of stressful experiences while receiving prolonged mechanical ventilation in an intensive care unit. Critical care medicine. 2002;30(4):746-52.
3. Lewandowska K, Mędrzycka-Dąbrowska W, Pilch D, Wach K, Fortunato A, Krupa S, et al. Sleep Deprivation from the Perspective of a Patient Hospitalized in the Intensive Care Unit-Qualitative Study. Healthcare (Basel). 2020;8(3):351.
4. Puntillo K, Arai S, Cohen N, Gropper M, Neuhaus J, Paul S, et al. Symptoms experienced by intensive care unit patients at high risk of dying. Critical care medicine. 2010;38(11):2155-60.
5. Topcu S, Alpar S, Karabacak B, Kebapcı A. Patient experiences in intensive care units: a systematic review. Patient Experience Journal. 2017;4:115-27.
6. Tate JA. Anxiety and Agitation in Mechanically Ventilated Patients. 2012;22(2):157-73.
7. Tanaka LMS, Azevedo LCP, Park M, Schettino G, Nassar AP, Réa-Neto A, et al. Early sedation and clinical outcomes of mechanically ventilated patients: a prospective multicenter cohort study. Critical Care. 2014;18(4):R156.
8. Litton E, Carnegie V, Elliott R, Webb SA. The Efficacy of Earplugs as a Sleep Hygiene Strategy for Reducing Delirium in the ICU: A Systematic Review and Meta-Analysis. Critical care medicine. 2016;44(5):992-9.

9. Lof L, Berggren L, Ahlstrom G. ICU patients' recall of emotional reactions in the trajectory from falling critically ill to hospital discharge: follow-ups after 3 and 12 months. Intensive & critical care nursing. 2008;24(2):108-21.

10. Nikayin S, Rabiee A, Hashem MD, Huang M, Bienvenu OJ, Turnbull AE, et al. Anxiety Symptoms in Survivors of Critical Illness: A Systematic Review and Meta-Analysis. General hospital psychiatry. 2016;43:23-9.

11. Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJC, Pandharipande PP, et al. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Critical care medicine. 2018;46(9):e825-e73.

12. Robb SL, Burns DS, Carpenter JS. Reporting guidelines for music-based interventions. J Health Psychol. 2011;16(2):342-52.

13. Dileo C. A Proposed Model For Identifying Practices A Content Analysis of the First 4 Years of Music and Medicine. Music and medicine. 2013;5:110-8.

14. Richard-Lalonde M, Gélinas C, Boitor M, Gosselin E, Feeley N, Cossette S, et al. The Effect of Music on Pain in the Adult Intensive Care Unit: A Systematic Review of Randomized Controlled Trials. Journal of Pain and Symptom Management. 2020;59(6):1304-19.e6.

15. Bradt J, Dileo C. Music interventions for mechanically ventilated patients. The Cochrane database of systematic reviews. 2014;2014(12):Cd006902.

16. Grap M, Munro C, Wetzel P, Best A, Ketchum J, Hamilton V, et al. Sedation in adults receiving mechanical ventilation: physiological and comfort outcomes. Am J Crit Care. 2012;21(3):e53-63; quiz e4.

17. Gélinas C, Puntillo KA, Joffe AM, Barr J. A validated approach to evaluating psychometric properties of pain assessment tools for use in nonverbal critically ill adults. Semin Respir Crit Care Med. 2013;34(2):153-68.

18. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med. 2002;166(10):1338-44.

19. Thayer JF, Lane RD. A model of neurovisceral integration in emotion regulation and dysregulation. Journal of affective disorders. 2000;61(3):201-16.

20. Hagemann D, Waldstein SR, Thayer JF. Central and autonomic nervous system integration in emotion. Brain and cognition. 2003;52(1):79-87.

21. Kreibig SD. Autonomic nervous system activity in emotion: a review. Biological psychology. 2010;84(3):394-421.

22. McCorry LK. Physiology of the autonomic nervous system. Am J Pharm Educ. 2007;71(4):78-.

23. Zatorre RJ. Musical pleasure and reward: mechanisms and dysfunction. Annals of the New York Academy of Sciences. 2015;1337:202-11.

24. Farnsworth P. The Social Psychology of Music. 2nd ed. Ames, Iowa: The Iowa State University Press 1969. 298 p.

25. Fancourt D, Ockelford A, Belai A. The psychoneuroimmunological effects of music: a systematic review and a new model. Brain, behavior, and immunity. 2014;36:15-26.

26. Kaul H, Bharti N. Monitoring Depth of Anaesthesia. Indian Journal of Anaesthesia. 2002;46(4):323-.

27. Damasio A. Descartes' Error. Emotion, Reason, and the Human Brain. New York: Grosset Putnam; 1994.

28. van den Bosch I, Salimpoor VN, Zatorre RJ. Familiarity mediates the relationship between emotional arousal and pleasure during music listening. Frontiers in Human Neuroscience. 2013;7:534.

29. Guyon A, Studer RK, Hildebrandt H, Horsch A, Nater UM, Gomez P. Music performance anxiety from the challenge and threat perspective: psychophysiological and performance outcomes. BMC psychology. 2020;8(1):87.

30. Mellott KG, Grap MJ, Munro CL, Sessler CN, Wetzel PA. Patient-ventilator dyssynchrony: clinical significance and implications for practice. Critical care nurse. 2009;29(6):41-55.

31. Liang Z, Ren DX, Choi JY, Happ MB, Hravnak M, Hoffman LA. Music intervention during daily weaning trials-A 6 day prospective randomized crossover trial. Complementary therapies in medicine. 2016;29:72-7.

32. Wong HL, Lopez-Nahas V, Molassiotis A. Effects of music therapy on anxiety in ventilator-dependent patients. Heart & lung : the journal of critical care. 2001;30(5):376-87.

33. Almerud S, Petersson K. Music therapy--a complementary treatment for mechanically ventilated intensive care patients. Intensive & critical care nursing. 2003;19(1):21-30.

34. Beaulieu-Boire G, Bourque S, Chagnon F, Chouinard L, Gallo-Payet N, Lesur O. Music and biological stress dampening in mechanically-ventilated patients at the intensive care unit ward-a prospective interventional randomized crossover trial. Journal of critical care. 2013;28(4):442-50.

35. Damshens MH, Sanie MS, Javadpour S, Khaef MA, Rastgarian A. The Role of Music on the Delirium in Traumatic Patients: A Case Study in the ICU of Peymanieh Hospital of Jahrom, Fars Province, Iran. Ambient Science. 2018;5:97-101.

36. Dijkstra BM, Gamel C, van der Bijl JJ, Bots ML, Kesecioglu J. The effects of music on physiological responses and sedation scores in sedated, mechanically ventilated patients. Journal of clinical nursing. 2010;19(7-8):1030-9.

37. Chlan L. Effectiveness of a music therapy intervention on relaxation and anxiety for patients receiving ventilatory assistance. Heart & lung : the journal of critical care. 1998;27(3):169-76.

38. Han L, Li JP, Sit JW, Chung L, Jiao ZY, Ma WG. Effects of music intervention on physiological stress response and anxiety level of mechanically ventilated patients in China: a randomised controlled trial. J Clin Nurs. 2010;19(7-8):978-87.

39. Jaber S, Bahloul H, Guétin S, Chanques G, Sebbane M, Eledjam JJ. Effects of music therapy in intensive care unit without sedation in weaning patients versus non-ventilated patients. Annales Francaises d'Anesthesie et de Reanimation. 2007;26(1):30-8.

40. Jacq G, Melot K, Bezou M, Foucault L, Courau-Courtois J, Cavelot S, et al. Music for pain relief during bed bathing of mechanically ventilated patients: A pilot study. PloS one. 2018;13(11):e0207174.

41. Korhan EA, Khorshid L, Uyar M. The effect of music therapy on physiological signs of anxiety in patients receiving mechanical ventilatory support. Journal of Clinical Nursing. 2011;20(7-8):1026-34.

42. Lee OK, Chung YF, Chan MF, Chan WM. Music and its effect on the physiological responses and anxiety levels of patients receiving mechanical ventilation: a pilot study. J Clin Nurs. 2005;14(5):609-20.

43. Mateu-Capell M, Arnau A, Juvinya D, Montesinos J, Fernandez R. Sound isolation and music on the comfort of mechanically ventilated critical patients. Nursing in critical care. 2019;24(5):290-8.

44. Messika J, Martin Y, Maquigneau N, Henry-Laguarrigue M, Puechberty C, Stoclin A, et al. Effect of a musical intervention on tolerance and efficacy of non-invasive ventilation: The "MUSique pour L'Insuffisance Respiratoire Aigue-MUS-IRA" randomized controlled trial. Annals of Intensive Care. 2017;7(1):22-3.

45. Liang Z, Ren D, Choi J, Happ MB, Hravnak M, Hoffman LA. Music intervention during daily weaning trials-A 6-day prospective randomized crossover trial. Complementary therapies in medicine. 2016;29:72-7.

46. Lee CH, Lee CY, Hsu MY, Lai CL, Sung YH, Lin CY, et al. Effects of Music Intervention on State Anxiety and Physiological Indices in Patients Undergoing Mechanical Ventilation in the Intensive Care Unit. Biol Res Nurs. 2017;19(2):137-44.

47. Liang Z, Ren D, Choi J, Happ MB, Hravnak M, Hoffman LA. Music intervention during daily weaning trials—A 6 day prospective randomized crossover trial. Complementary therapies in medicine. 2016;29:72-7.

48. Synn A, Choe MA, editors. Effect of Music Therapy on the Physiological Index, Anxiety and Dyspnea of Patients with Mechanical Ventilator Weaning2012.

49. Vaporidi K, Akoumianaki E, Telias I, Goligher EC, Brochard L, Georgopoulos D. Respiratory Drive in Critically Ill Patients: Pathophysiology and Clinical Implications. Am J Respir Crit Care Med. 2019.

50. Team RC. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2021 [Available from: https://www.R-project.org/.

51. Wilcox R. Chapter 2 - A Foundation for Robust Methods. In: Wilcox R, editor. Introduction to Robust Estimation and Hypothesis Testing (Fourth Edition): Academic Press; 2017. p. 25-43.

52. Bates D, Mächler M, Bolker B, Walker S. Fitting Linear Mixed-Effects Models Using lme4. Journal of Statistical Software. 2015;67(1):1 - 48.

53. Aktas Y, Karabulut N. The effects of music therapy in endotracheal suctioning of mechanically ventilated patients. Nursing in critical care. 2016;21(1):44-52.

54. Aktas Y, Karabulut N. Relief of Procedural Pain in Critically Ill Patients by Music Therapy: A Randomized Controlled Trial. Complementary medicine research. 2019:1-9.

55. Habibi A, Damasio A. Music, feelings, and the human brain. US: Educational Publishing Foundation; 2014. p. 92-102.

56. Jäncke L. Music, memory and emotion. J Biol. 2008;7(6):21-.

57. Särkämö T, Soto D. Music listening after stroke: beneficial effects and potential neural mechanisms. Annals of the New York Academy of Sciences. 2012;1252:266-81.

58. Koutsoukou A, Katsiari M, Orfanos SE, Kotanidou A, Daganou M, Kyriakopoulou M, et al. Respiratory mechanics in brain injury: A review. World journal of critical care medicine. 2016;5(1):65-73.

59. North JB, Jennett S. Abnormal Breathing Patterns Associated With Acute Brain Damage. Archives of Neurology. 1974;31(5):338-44.

60. Koelsch S, Fuermetz J, Sack U, Bauer K, Hohenadel M, Wiegel M, et al. Effects of Music Listening on Cortisol Levels and Propofol Consumption during Spinal Anesthesia. Frontiers in psychology. 2011;2:58.

61. Nowak H, Zech N, Asmussen S, Rahmel T, Tryba M, Oprea G, et al. Effect of therapeutic suggestions during general anaesthesia on postoperative pain and opioid use: multicentre randomised controlled trial. BMJ (Clinical research ed). 2020;371:m4284.

62. Bansal P, Kharod U, Patel P, Sanwatsarkar S, Patel H, Kamat H. The effect of music therapy on sedative requirements and haemodynamic parameters in patients under spinal anaesthesia; A prospective study. Journal of Clinical and Diagnostic Research. 2010;4(4):2782-9.

63. Kahloul M, Mhamdi S, Nakhli MS, Sfeyhi AN, Azzaza M, Chaouch A, et al. Effects of music therapy under general anesthesia in patients undergoing abdominal surgery. The Libyan journal of medicine. 2017;12(1):1260886.

64. Pattinson KT. Opioids and the control of respiration. British journal of anaesthesia. 2008;100(6):747-58.

65. Blouin RT, Seifert HA, Babenco HD, Conard PF, Gross JB. Propofol depresses the hypoxic ventilatory response during conscious sedation and isohypercapnia. Anesthesiology. 1993;79(6):1177-82.

66. De Oliveira GS, Jr., Fitzgerald PC, Hansen N, Ahmad S, McCarthy RJ. The effect of ketamine on hypoventilation during deep sedation with midazolam and propofol: a

randomised, double-blind, placebo-controlled trial. Eur J Anaesthesiol. 2014;31(12):654-62.

67. Mildh L, Taittonen M, Leino K, Kirvelä O. The effect of low-dose ketamine on fentanyl-induced respiratory depression. Anaesthesia. 1998;53(10):965-70.

68. Mortero RF, Clark LD, Tolan MM, Metz RJ, Tsueda K, Sheppard RA. The Effects of Small-Dose Ketamine on Propofol Sedation: Respiration, Postoperative Mood, Perception, Cognition, and Pain. Anesthesia & Analgesia. 2001;92(6).

69. Grover S, Sharma A, Aggarwal M, Mattoo SK, Chakrabarti S, Malhotra S, et al. Comparison of symptoms of delirium across various motoric subtypes. Psychiatry and clinical neurosciences. 2014;68(4):283-91.

70. Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Critical care medicine. 2001;29(7):1370-9.

71. Khan SH, Xu CJ, Purpura R, Durrani S, Lindroth H, Wang S, et al. DECREASING DELIRIUM THROUGH MUSIC: A RANDOMIZED PILOT TRIAL. American Journal of Critical Care. 2020;29(2):E31-E8.

72. La G, Gerdner L. Evidence-Based Guideline: Individualized Music in Persons with Dementia (6th Edition). 2019.

73. Cardozo M. Harmonic sounds: complementary medicine for the critically ill. Br J Nurs. 2004;13(22):1321-4.

74. White JM. State of the science of music interventions. Critical care and perioperative practice. Crit Care Nurs Clin North Am. 2000;12(2):219-25.

75. Allen K, Golden LH, Izzo JL, Jr., Ching MI, Forrest A, Niles CR, et al. Normalization of hypertensive responses during ambulatory surgical stress by perioperative music. Psychosomatic medicine. 2001;63(3):487-92.

76. Heiderscheit A, Chlan L, Donley K. Instituting a music listening intervention for critically ill patients receiving mechanical ventilation: Exemplars from two patient cases. Music and medicine. 2011;3(4):239-46.

77. Heiderscheit A, Breckenridge SJ, Chlan LL, Savik K. Music preferences of mechanically ventilated patients participating in a randomized controlled trial. Music and medicine. 2014;6(2):29-38.

78. Chlan L, Weinert C, Heiderscheit A, Skaar D, Tracy MF, Savik K. Effects of patient-initiated music listening on anxiety in mechanically ventilated patients. Critical care medicine. 2011;39:13.

79. Park S, Williams RA, Lee D. Effect of Preferred Music on Agitation After Traumatic Brain Injury. Western journal of nursing research. 2016;38(4):394-410.

80. Jong Yoen P, Soohyun P. Effects of Two Music Therapy Methods on Agitation and Anxiety among Patients Weaning off Mechanical Ventilation: A Pilot Study. Journal of Korean Academy of Fundamentals of Nursing. 2019;26(2):136-43.

81. Chanques G, Kress JP, Pohlman A, Patel S, Poston J, Jaber S, et al. Impact of ventilator adjustment and sedation-analgesia practices on severe asynchrony in patients ventilated in assist-control mode. Critical care medicine. 2013;41(9):2177-87.

82. van den Bosch OFC, Alvarez-Jimenez R, de Grooth H-J, Girbes ARJ, Loer SA. Breathing variability—implications for anaesthesiology and intensive care. Critical Care. 2021;25(1):280.

83. Tipton MJ, Harper A, Paton JFR, Costello JT. The human ventilatory response to stress: rate or depth? The Journal of physiology. 2017;595(17):5729-52.

84. Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. The New England journal of medicine. 1991;324(21):1445-50.

85. Kallet RH, Hemphill JC, 3rd, Dicker RA, Alonso JA, Campbell AR, Mackersie RC, et al. The spontaneous breathing pattern and work of breathing of patients with acute respiratory distress syndrome and acute lung injury. Respiratory care. 2007;52(8):989-95.

86. Smoller JW, Pollack MH, Otto MW, Rosenbaum JF, Kradin RL. Panic anxiety, dyspnea, and respiratory disease. Theoretical and clinical considerations. Am J Respir Crit Care Med. 1996;154(1):6-17.

87. Banzett RBB, Sheridan AR, Baker KM, Lansing RW, Stevens JP. 'Scared to death' dyspnoea from the hospitalised patient's perspective. BMJ open respiratory research. 2020;7(1).

88. Kallet RH. Patient-ventilator interaction during acute lung injury, and the role of spontaneous breathing: part 1: respiratory muscle function during critical illness. Respiratory care. 2011;56(2):181-9.

89. Kallet RH, Katz JA. Respiratory system mechanics in acute respiratory distress syndrome. Respiratory care clinics of North America. 2003;9(3):297-319.

Chapter 5: Conclusion

This dissertation study contributes to the growing body of research examining the use of recorded music listening interventions (RMLIs) to manage distressing symptoms experienced during critical care and in particular during mechanical ventilation (MV). Broadly, this dissertation summarizes the state of the science, while pointing out gaps in the literature that addresses RMLIs for symptom management through review of prior works, a qualitative analysis, and the examination of a novel, objective measure of the effect of an RMLI during MV. This chapter will conclude the dissertation by summarizing key research findings and discussing the significance thereof. The dissertation findings will then be contextualized against relevant theories. Next, limitations to the research will be considered. Finally, opportunities for future research and nursing practice will be presented.

AIM 1: The systematic review of the literature confirmed that RMLIs are effective for the treatment of anxiety and pain and identified other common symptoms such as agitation, that may be moderated by RMLIs in adults during MV. The broad scope of this review did not allow for summative recommendations of RMLIs due to the wide variety of experienced symptoms but does highlight important literature gaps. Specifically, few studies measure the effect of RMLIs on common symptoms such as dyspnea, confusion, delirium, sleep, loneliness and general distress. The heterogeneity of outcome measures also made it difficult to synthesize the results. In general, studies that measured a symptom outcome with a self-report of symptom experience or a validated instrument demonstrated consistent RMLI results. Studies that included proxy measures of symptoms such as vital signs did not show effects. Music selections in the review were mostly consistent in their structure. Most music was delivered via headphones for 20-60

minutes, was described as ‘relaxing’ music, with slow tempos including the music selected by investigators and from the limited patient choices. Two thirds of the reviewed studies were at moderate to high risk of bias using the Evidence Project risk of bias tool (1), limiting the strength of any study conclusions.

AIM 2: The qualitative analysis examined the perceptions of the effects of listening to personally selected music during critical care hospitalization and MV suggest that listening to music may be beneficial for cognitive and psychological recovery. Six themes emerged from the analysis of 14 semi-structured interviews, notes and observations made during a 16-month study period in a surgical and neuro-trauma ICU. Participants described that listening to personally selected, recorded music during their critical care hospitalization was helpful because it: 1) Restored their consciousness; 2) Maintained their cognition; 3) Humanized their hospital experience; 4) Provided a source of connection; 5) Improved their psychological wellbeing; and 6) Resolved the problems of silence. Social and demographic patient information and type of preferred music varied. However, perception of the psychological and cognitive benefits of music listening was consistent across the group. The generalizability of the findings are limited due to the number of informants, and the single center experience. However, the study highlights an under-examined use of RMLI critically ill MV adults for treatment of symptoms associated with cognition and psychological wellbeing, both which may affect other common symptoms in this vulnerable population.

AIM 3: Breathing measures associated with relaxation did not vary as hypothesized with a MLI in this pilot study of 16 MV adults during both machine-controlled ventilation and spontaneous breathing modalities. Analysis of breath-by-breath data did not demonstrate effect on respiratory rate (breaths per minute), breath depth (tidal volume in liters or maximum pressure associated

with fixed volume breaths), nor breath pattern (liters breath per minute, breaths per liter per minute, inspiratory flow, and other indirect measures of work of breathing). The null results in this pilot were likely related to the large observed variance within the small sample, high incidence of delirium, and the heterogeneity of the music selections in the intervention. Use of the NM3® (Philips, Carlsbad, CA) noninvasive pulmonary mechanics monitor facilitated the collection of objective, rich, continuous data and is a feasible instrument that adds to the rigor of the findings.

Synthesis of Findings:

This dissertation study aimed to identify symptoms that may be moderated by listening to recorded music during MV in critical care and potential measures of the effects of RMLIs to support an evidence-based expansion of the use of RMLIs for MV adults. Our findings indicate that the potential benefits of listening to recorded music during MV have been under-measured in the past, where the majority of studies examining the effects of RMLI focus specifically on outcomes of pain or anxiety. These observations were confirmed in the qualitative analysis where we learned that patients used music listening to treat a variety of cognitive and psychological symptoms (e.g., loneliness, fear, stress, de-situation, dehumanization) including some which may predict or cause long term morbidity. Study participants rarely described the use of music listening for pain or anxiety experiences. Instead, participants explained that they used music listening to address fear, loneliness, confusion, de-situation, and dehumanization, and sleep disturbances all potential contributors to development of post-traumatic stress disorder and post-intensive care unit syndrome (2, 3). Results of the qualitative study also showed that patients experienced distressing symptoms as co-occurring and interactive experiences, as is consistent with previous symptom research in this population (4, 5). Participants grouped their

symptoms together describing how their symptoms interacted with one another and how music helped them to manage their symptom burden holistically. These findings suggest that studies designed to measure the effect of RMLIs on single symptoms in critically ill MV adults, may miss the broader benefits of RMLIs.

The results of this dissertation also support the view that listening to recorded music is associated with improved self-report of symptom experience and is an acceptable intervention for people experiencing MV and critical care hospitalization. Self-reported pain, anxiety, dyspnea and distress scores were all improved with music listening interventions in the systematic review. Participants in the qualitative study described several psychological and cognitive symptoms that were moderated by listening to music and reported that listening to recorded music had been of unique benefit to them as they recovered. In the quantitative analysis, we experienced wide acceptability of the intervention, with only one person declining a RMLI during the whole study period, and several more requesting to listen to recorded music than could be enrolled in this small pilot study.

Objective measurements of the effects of RMLIs were less conclusive in this study. On the one hand, the use of validated psychometric instruments were a strength in several studies included in the review. However, physiological measures of the effects of MLI in MV adults remain undetermined. In the systematic review, we found that mean values of vital signs such as heart rate, blood pressure and respiratory rate did not vary with MLIs. We hypothesized that a more discrete, and theoretically grounded measurement, such as continuous breath by breath data derived from the ventilator may demonstrate an effect of MLI. We were unable to detect a difference in any breathing measures in either group of ventilated patients (ventilator-controlled or spontaneous breaths).

Significance of Findings:

This dissertation provides a foundation to explore new measures of the effects of RMLI in MV adults. Specifically, the findings of this dissertation support the use of RMLI for treatment of psychological and cognitive symptoms for which there are few feasible therapies in ICU , and which contribute significantly to overall morbidity. Critically ill and MV adults experience fear, confusion, hallucination, loneliness, distress, lack of sleep, depression and cognitive impairment (4-7). Each of these symptoms may extend length of MV, length of stay and can increase the likelihood of a person developing delirium, post-traumatic stress disorder or post intensive care syndrome after discharge (2, 3, 8, 9). The use of MLI to treat the psychological and cognitive symptoms experienced during critical illness and MV has the potential to impact both short-and long-term outcomes.

Communication barriers of critical illness and MV make many cognitive behavioral therapies designed to treat psychological symptoms unfeasible. However, the findings of this study suggests that patients perceive a cognitive and psychological benefit from listening to music even while semi-conscious or unable to communicate. The validity of this hypothesis will need to be tested in future studies. However, there is precedent in the literature that examines the effects of RMLI on consciousness among adults with disorders of consciousness (10, 11). Coupled with this, long term studies of people with brain injury show that both mood and cognition are improved with RMLI (12, 13).

The heterogeneity of the outcome measures in the systematic review highlights the need for standardization in reporting of symptom outcomes. Fortunately, there exist several validated measures to examine many of the newly identified and understudied symptoms mentioned in this dissertation. Quality and quantity of sleep in critical care can be measured with the Sleep

Observation Tool and the Richards Campbell Sleep Questionnaire (14). Psychological distress can be measured with the hospital anxiety and depression scale (HADS) or the intensive care psychological assessment tool (15). There are still a lack of reliable physiological outcome measures to demonstrate the effectiveness of RMLI among the critically ill. Reliance on physiological signs such as vital signs to demonstrate symptom outcome is problematic in critical care studies. Measures such as mean heart rate have not been shown to be reliable biomarkers to assess subtle affective changes in most RMLI studies to date (16). The use of validated measures of symptoms in studies of RMLI are therefore recommended to clarify the potential uses in MV adults. Standardization of the reporting of symptom outcome measures to include validated instruments will also allow for comparisons and synthesis of future. Furthermore, the use of validated scales and psychometric instruments will help generate clinically meaningful and comparable results.

Diversity of participants and emphasis on preferred, personally selected music are an additional study strength. The significance of preferred, personally selected music has been recommended for decades in un-tested guidelines for the use of RMLI for symptom management in acute care and critical care in particular (17-22). Listening to music may have effects on the limbic and hypothalamic-pituitary axis resulting in physical signs and psychological reports of relaxation, anxiolysis, and emotional reward (23-25). This mechanism is thought to be activated by an emotional response to music, based on memories of music and cognitive processing of musical stimuli (26, 27). People demonstrate wide variety in their musical preferences and report increased pleasure response to preferred or familiar music (27). Importantly, the bases of our musical preferences are rooted in our social and cultural context (24, 26, 28, 29). Despite these recommendations most research that explores the effects of RMLI tests the effects of

investigator-selected music or restricts choice of patient-selected music to genres, tempos, and moods that investigators deem suitable. In the systematic review, we found that unrestricted music choice was associated with improved overall symptom experience. During the qualitative interviews, patients, their families, and friends explained that personally selected music had benefit beyond what could be measured as a discrete symptom. Music selections in older studies of RMLI have been restricted to CDs and cassette tapes but advances in technology now allow for increased access to preferred music selections through the use of web-based music libraries and bedside tablets. In both the qualitative and quantitative studies, we observed a diverse group of patients and families making a wide variety of music selections using tablets at the bedside including languages other than English. Diversification of participants and music selections are needed in RMLI studies in the United States where the majority of prior research examining RMLI has focused on middle aged and older white participants (30-33). Beyond increasing the generalizability of findings, inclusion of a more diverse sample of patients and unrestricted music selections may also lead to improvements in outcomes and hospital experiences in racial and ethnic minority populations who may experience unique psychological challenges associated with hospitalization, have higher morbidity than their white counterparts and who have been marginalized from past research (34-36).

Theoretical Framework:

This dissertation was informed by two theories, Florence Nightingale's Theory of Nursing (and the Environment) and Antonio Damasio's Theory of Emotion, Feeling and Core Consciousness (26, 37). Damasio believes that physical and emotional survival (homeostasis) is dependent on the relationship between feelings (primary emotions), emotions (secondary emotions) and consciousness (26). According to Damasio, (primary emotions originate in the in

the body proper, secondary emotions originate in the brain and consciousness is developed in the mind. The origins of primary emotions are from sensory stimuli which generate a series of signals in the brain, and which act on the body proper. Secondary emotions represent a cerebral (or brain based) analysis of feelings and other stimuli; they are in effect a neural map, a web of interactions that develop in response to stimuli from the internal or external environment. Applying Damasio's theory, music, a provocative sensory stimulus is processed in the mind and informs the neural network responsible for emotions and feelings, thereby resulting in alterations to both our conscious experience and our somatic state.

Fundamental tenets of Nightingale's theory are that disease is a "reparative process" and that environmental imbalances impair restoration of a state of wellness or balance within a person often leading to extra suffering. Nightingale believes that nurses ought to assist this reparative process by correcting imbalances *surrounding* the patient. In each of Nightingale's (1859/1980) recommendations, the patient is center, and great emphasis is placed on the influence of the physical and psychological environment of the patient's wellbeing. Like Damasio, Nightingale recognized the effect of sensory input and memory on physical and psychological wellbeing. Nightingale advocated for the use of music, as an environmental stimulus to help restore mind and body balance. In *Notes on Nursing*, Nightingale also cautioned against reliance on a singular symptom or sign to assess an individual's wellbeing, explaining that improved sleep may improve pain, delirium and anxiety (37).

The findings from this dissertation align well with both theories and are best illustrated in the qualitative analysis. In that study, participants described a series of physical and emotional responses to music stimuli based on their memories associated with their personally chosen music. Participants explained that listening to music stimulated their minds through prior

exposures (memories), and that this stimulation served as a trigger to awaken their mind into consciousness. Once conscious, listening to music helped participants manage their thoughts through reflection, distraction, and processing. Critically, participants described feeling that music listening helped them to achieve cognitive, psychological and physical balance (homeostasis). Some felt 'music had saved their [sic] life'. Damasio's and Nightingale's Holism also acknowledges the complex and integrated nature of the symptoms experienced by participants in the qualitative study and support taking a wider view of the symptom experience of critically ill, MV adults.

Limitations of the Research:

This dissertation has several limitations. First both the qualitative and quantitative analyses were conducted with small samples, at a single site, limiting the generalizability of findings from either study. The qualitative analysis was designed to be hypothesis generating, and the findings may be specific to the individuals sampled or the setting in which they were hospitalized. In the quantitative analysis, we examined the feasibility of a novel measurement. While theoretically supported, this measure may not be reliable in such a confounded environment. Therefore, findings from this dissertation should only be used to inform future larger, multi center trials and should not be used to generalize to larger populations. The clinical heterogeneity and diversity of music selections in these studies present another limitation to the work. Similarly, the broad scope of the review and the heterogeneity of outcomes and measurements, limited our ability to make any summary recommendations from the analysis. This research was limited by time and personnel constraints, as all data collection was completed by one person, in a short period of time. Finally, this research was conducted in a critical care unit during the Covid-19 Pandemic. Patients hospitalized during the pandemic

experienced extreme levels of separation due to strict visitation policies which may have influenced the results. Patient screening, enrollment and implementation was also affected by strained staffing resources and other restrictions related to infection control.

Implications for Research:

Findings from this dissertation can be used to support future research that expands the symptoms of interest for RMLIs to include clinically meaningful outcomes as identified in the qualitative study such as consciousness, distress, sleep, mood, incidence and severity of delirium, cognitive impairment and acute stress. The lack of reliable physiological outcome measures also highlights the need for further research to identify potential biomarkers for response to RMLI in critical care. The wide variety of music selections in our small, but diverse sample of patients challenges prior recommendations that limit the tempo, mood and genre of music selections in critical care. Future studies that examine the varied types of music in selections made by diverse samples will contribute to growing understandings of how people benefit from listening to music during critical care hospitalization.

Implications for Practice:

This research indicates that recorded RMLIs are an acceptable, feasible tool for nurses to use to improve the symptom experience of MV adults during critical care hospitalization. As an adjunctive intervention, playing recorded music may help nurses to reduce overall medication use while maintaining adequate relief of pain and anxiety. Importantly, RMLI are a low-risk tool to help manage other co-occurring symptoms not amenable to medications such as sleep, delirium, fear and depression. Nurses can initiate music listening even when patients are sedated, which has been identified by nurses as a barrier to implementation of cognitive stimulation in ICU (38). Engaging families to help choose music for patients unable to communicate is also a

patient and family centered practice that can increase communication and empowerment of patients and their families during critical care hospitalization, which may reduce length of stay, incidence of delirium and post-intensive care syndrome (39). Seeking patient and family participation in health care is an important step towards building an equitable and culturally humble practice (40, 41). Culturally humble care which is informed by cultural identity, personal preferences, history and context may also help to reduce health inequities and restore health after injury (42).

Conclusion:

The morbidity associated with the symptoms experienced during MV makes it an imperative to expand the access and use of non-pharmacologic interventions for adults during critical care hospitalization. Listening to preferred, personally selected music represents a safe, equitable intervention that is likely to be of benefit for the management of common psychological and cognitive symptoms not amenable to traditional medical interventions. Future studies that use validated instruments and clinically meaningful outcomes will provide scientific justification for the use of RMLI and to contribute to the understanding of the mechanism of action of RMLI.

References

1. Kennedy CE, Fonner VA, Armstrong KA, Denison JA, Yeh PT, O'Reilly KR, et al. The Evidence Project risk of bias tool: assessing study rigor for both randomized and non-randomized intervention studies. Systematic Reviews. 2019;8(1):3.
2. Nikayin S, Rabiee A, Hashem MD, Huang M, Bienvenu OJ, Turnbull AE, et al. Anxiety Symptoms in Survivors of Critical Illness: A Systematic Review and Meta-Analysis. General hospital psychiatry. 2016;43:23-9.
3. Lof L, Berggren L, Ahlstrom G. ICU patients' recall of emotional reactions in the trajectory from falling critically ill to hospital discharge: follow-ups after 3 and 12 months. Intensive & critical care nursing. 2008;24(2):108-21.
4. Puntillo K, Arai S, Cohen N, Gropper M, Neuhaus J, Paul S, et al. Symptoms experienced by intensive care unit patients at high risk of dying. Critical care medicine. 2010;38(11):2155-60.
5. Topcu S, Alpar S, Karabacak B, Kebapcı A. Patient experiences in intensive care units: a systematic review. Patient Experience Journal. 2017;4:115-27.
6. Granberg A, Bergbom Engberg I, Lundberg D. Patients' experience of being critically ill or severely injured and cared for in an intensive care unit in relation to the ICU syndrome. Part I. Intensive & critical care nursing. 1998;14(6):294-307.
7. Rotondi AJ, Chelluri L, Sirio C, Mendelsohn A, Schulz R, Belle S, et al. Patients' recollections of stressful experiences while receiving prolonged mechanical ventilation in an intensive care unit. Critical care medicine. 2002;30(4):746-52.
8. Zaal IJ, Devlin JW, Peelen LM, Slooter AJ. A systematic review of risk factors for delirium in the ICU. Critical care medicine. 2015;43(1):40-7.

9. Von Rueden KT, Wallizer B, Thurman P, McQuillan K, Andrews T, Merenda J, et al. Delirium in Trauma Patients: Prevalence and Predictors. Crit Care Nurse. 2017;37(1):40-8.
10. Sun J, Chen W. Music therapy for coma patients: preliminary results. European review for medical and pharmacological sciences. 2015;19(7):1209-18.
11. Rahimi F, Saleh, K., Seidi, J. . The effect of pleasant audio stimulation on the level of consciousness of comatose patient: a randomized clinical trial. Acta Medica Meditterranea Acta Medica Meditterranea 2019;35:985-9.
12. Phipps MA, Carroll DL, Tsiantoulas A. Music as a Therapeutic Intervention on an Inpatient Neuroscience Unit. Complementary therapies in clinical practice. 2010;16(3):138-42.
13. Siponkoski ST, Martínez-Molina N, Kuusela L, Laitinen S, Holma M, Ahlfors M, et al. Music Therapy Enhances Executive Functions and Prefrontal Structural Neuroplasticity after Traumatic Brain Injury: Evidence from a Randomized Controlled Trial. Journal of neurotrauma. 2020;37(4):618-34.
14. Richards KC, Wang Y-y, Jun J, Ye L. A Systematic Review of Sleep Measurement in Critically Ill Patients. Frontiers in Neurology. 2020;11.
15. Mason N, Egan D, O'Loghlen S, Conway D. Measuring anxiety & depression in the post critical care population - comparison of the hospital anxiety and depression scale and intensive care psychological assessment tool. Intensive Care Medicine Experimental. 2015;3(Suppl 1):A963.
16. Ellis RJ, Thayer JF. Music and Autonomic Nervous System (Dys)function. Music perception. 2010;27(4):317-26.
17. La G, Gerdner L. Evidence-Based Guideline: Individualized Music in Persons with Dementia (6th Edition). 2019.

18. Cardozo M. Harmonic sounds: complementary medicine for the critically ill. Br J Nurs. 2004;13(22):1321-4.

19. White JM. State of the science of music interventions. Critical care and perioperative practice. Crit Care Nurs Clin North Am. 2000;12(2):219-25.

20. Allen K, Golden LH, Izzo JL, Jr., Ching MI, Forrest A, Niles CR, et al. Normalization of hypertensive responses during ambulatory surgical stress by perioperative music. Psychosomatic medicine. 2001;63(3):487-92.

21. Heiderscheit A, Chlan L, Donley K. Instituting a music listening intervention for critically ill patients receiving mechanical ventilation: Exemplars from two patient cases. Music and medicine. 2011;3(4):239-46.

22. Fontaine DK. Nonpharmacologic management of patient distress during mechanical ventilation. Critical care clinics. 1994;10(4):695-708.

23. Zatorre RJ. Musical pleasure and reward: mechanisms and dysfunction. Annals of the New York Academy of Sciences. 2015;1337:202-11.

24. Farnsworth P. The Social Psychology of Music. 2nd ed. Ames, Iowa: The Iowa State University Press 1969. 298 p.

25. Fancourt D, Ockelford A, Belai A. The psychoneuroimmunological effects of music: a systematic review and a new model. Brain, behavior, and immunity. 2014;36:15-26.

26. Damasio A. Descartes' Error. Emotion, Reason, and the Human Brain. New York: Grosset Putnam; 1994.

27. van den Bosch I, Salimpoor VN, Zatorre RJ. Familiarity mediates the relationship between emotional arousal and pleasure during music listening. Frontiers in Human Neuroscience. 2013;7:534.

28. Zatorre R. Human perception: Amazon music. Nature. 2016;535(7613):496-7.

29. Oldfield BJ. When You Got the Yams-Kendrick Lamar and the Language of Power in Clinical Encounters. Jama. 2018;319(16):1642-3.

30. Chlan L. Effectiveness of a music therapy intervention on relaxation and anxiety for patients receiving ventilatory assistance. Heart & lung : the journal of critical care. 1998;27(3):169-76.

31. Chlan L, Engeland W, Anthony A, Guttormson J. Influence of music on the stress response in patients receiving mechanical ventilatory support: a pilot study. Am J Crit Care. 2007;16(2):141-5.

32. Chlan L, Weinert C, Heiderscheit A, Tracy M, Skaar D, Guttormson J, et al. Effects of patient-directed music intervention on anxiety and sedative exposure in critically ill patients receiving mechanical ventilatory support: a randomized clinical trial. Jama. 2013;309(22):2335-44.

33. Liang Z, Ren D, Choi J, Happ MB, Hravnak M, Hoffman LA. Music intervention during daily weaning trials—A 6-day prospective randomized crossover trial. Complementary therapies in medicine. 2016;29:72-7.

34. Alegria M, Canino G, Rios R, Vera M, Calderon J, Rusch D, et al. Inequalities in use of specialty mental health services among Latinos, African Americans, and non-Latino whites. Psychiatric services (Washington, DC). 2002;53(12):1547-55.

35. Roberts AL, Gilman SE, Breslau J, Breslau N, Koenen KC. Race/ethnic differences in exposure to traumatic events, development of post-traumatic stress disorder, and treatment-seeking for post-traumatic stress disorder in the United States. Psychological medicine. 2011;41(1):71-83.

36. Van Keer RL, Deschepper R, Huyghens L, Bilsen J. Mental well-being of patients from ethnic minority groups during critical care: a qualitative ethnographic study. BMJ open. 2017;7(9):e014075-e.

37. Nightingale F. Notes on Nursing. What It Is, And What It Is Not. Edinburgh: Churchill Livingstone; 1859/1980.

38. Parker AM, Aldabain L, Akhlaghi N, Glover M, Yost S, Velaetis M, et al. Cognitive Stimulation in an Intensive Care Unit: A Qualitative Evaluation of Barriers to and Facilitators of Implementation. Crit Care Nurse. 2021;41(2):51-60.

39. Marra A, Ely EW, Pandharipande PP, Patel MB. The ABCDEF Bundle in Critical Care. Critical care clinics. 2017;33(2):225-43.

40. Delphin-Rittmon ME, Andres-Hyman R, Flanagan EH, Davidson L. Seven essential strategies for promoting and sustaining systemic cultural competence. The Psychiatric quarterly. 2013;84(1):53-64.

41. Seeleman C, Essink-Bot ML, Stronks K, Ingleby D. How should health service organizations respond to diversity? A content analysis of six approaches. BMC health services research. 2015;15:510.

42. Brach C, Fraser I. Can cultural competency reduce racial and ethnic health disparities? A review and conceptual model. Medical care research and review : MCRR. 2000;57 Suppl 1:181-217

Publishing Agreement

It is the policy of the University to encourage open access and broad distribution of all theses, dissertations, and manuscripts. The Graduate Division will facilitate the distribution of UCSF theses, dissertations, and manuscripts to the UCSF Library for open access and distribution. UCSF will make such theses, dissertations, and manuscripts accessible to the public and will take reasonable steps to preserve these works in perpetuity.

I hereby grant the non-exclusive, perpetual right to The Regents of the University of California to reproduce, publicly display, distribute, preserve, and publish copies of my thesis, dissertation, or manuscript in any form or media, now existing or later derived, including access online for teaching, research, and public service purposes.

DocuSigned by:
Rebecca Menza
FF6859FD0849484...
Author Signature

5/24/2022
Date