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Effects of Patient-Directed Music Intervention on Anxiety and Sedative Exposure in Critically Ill Patients Receiving Mechanical Ventilatory Support A Randomized Clinical Trial

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CRITICALLY ILL MECHANICALLY ventilated patients receive intravenous sedative and analgesic medications to reduce anxiety and promote comfort and ventilator synchrony. These potent medications are often administered at high doses for prolonged periods and are associated with adverse effects such as bradycardia, hypotension, gut dysmotility, immobility, weakness, and delirium.¹⁻³ Despite protocols and sedation assessment tools that guide clinicians, patients still experience significant levels of anxiety.^{4,5}

Unrelieved anxiety and fear are not only unpleasant symptoms that clinicians want to palliate, but increased sympathetic nervous system activity can cause dyspnea and increased myocardial oxygen demand.⁶ Sustained anxiety and sympathetic nervous system activation can decrease the ability to concentrate, rest, or relax.^{6,7} Mechanically ventilated patients have little control over pharmacological interventions to relieve anxiety; dosing and frequency of sedative and analgesic medications are controlled by intensive care unit (ICU) clinicians. Interventions are

For editorial comment see p 2386.

Importance Alternatives to sedative medications, such as music, may alleviate the anxiety associated with ventilatory support.

Objective To test whether listening to self-initiated patient-directed music (PDM) can reduce anxiety and sedative exposure during ventilatory support in critically ill patients.

Design, Setting, and Patients Randomized clinical trial that enrolled 373 patients from 12 intensive care units (ICUs) at 5 hospitals in the Minneapolis-St Paul, Minnesota, area receiving acute mechanical ventilatory support for respiratory failure between September 2006 and March 2011. Of the patients included in the study, 86% were white, 52% were female, and the mean (SD) age was 59 (14) years. The patients had a mean (SD) Acute Physiology, Age and Chronic Health Evaluation III score of 63 (21.6) and a mean (SD) of 5.7 (6.4) study days.

Interventions Self-initiated PDM (n=126) with preferred selections tailored by a music therapist whenever desired while receiving ventilatory support, self-initiated use of noise-canceling headphones (NCH; n=122), or usual care (n=125).

Main Outcomes and Measures Daily assessments of anxiety (on 100-mm visual analog scale) and 2 aggregate measures of sedative exposure (intensity and frequency).

Results Patients in the PDM group listened to music for a mean (SD) of 79.8 (126) (median [range], 12 [0-796]) minutes/day. Patients in the NCH group wore the noise-abating headphones for a mean (SD) of 34.0 (89.6) (median [range], 0 [0-916]) minutes/day. The mixed-models analysis showed that at any time point, patients in the PDM group had an anxiety score that was 19.5 points lower (95% CI, -32.2 to -6.8) than patients in the usual care group (P=.003). By the fifth study day, anxiety was reduced by 36.5% in PDM patients. The treatment × time interaction showed that PDM significantly reduced both measures of sedative exposure. Compared with usual care, the PDM group had reduced sedation intensity by -0.18 (95% CI, -0.36 to -0.004) points/day (P=.05) and had reduced frequency by -0.21 (95% CI, -0.37 to -0.05) points/day (P=.01). The PDM group had reduced sedation frequency by -0.18 (95% CI, -0.36 to -0.004) points/day vs the NCH group (P=.04). By the fifth study day, the PDM patients received 2 fewer sedative doses (reduction of 38%) and had a reduction of 36% in sedation intensity.

Conclusions and Relevance Among ICU patients receiving acute ventilatory support for respiratory failure, PDM resulted in greater reduction in anxiety compared with usual care, but not compared with NCH. Concurrently, PDM resulted in greater reduction in sedation frequency compared with usual care or NCH, and greater reduction in sedation intensity compared with usual care, but not compared with NCH.

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needed that reduce anxiety, actively involve patients, and minimize the use of sedative medications.

Nonpharmacological interventions such as relaxing music are effective in reducing anxiety while reducing medication administration.^{8,9} Music is a powerful distractor that can alter perceived levels of anxiety¹⁰ by occupying attention channels in the brain with meaningful, auditory stimuli¹¹ rather than stressful environmental stimuli. Listening to preferred, relaxing music has reduced anxiety in mechanically ventilated patients in limited trials.¹²⁻¹⁵ It is not known if music can reduce anxiety throughout the course of ventilatory support, or reduce exposure to sedative medications. We evaluated if a patient-directed music (PDM) intervention could reduce anxiety and sedative exposure in ICU patients receiving mechanical ventilation.

METHODS

A 3-group, randomized clinical trial design was used. A computer-generated random numbers list allocated patients to 1 of 3 groups: (1) PDM intervention, (2) active control with noise-canceling headphones (NCH), or (3) usual care in the ICU. Group assignment was concealed in an opaque envelope. Patients were enrolled from 12 ICUs at 5 hospitals in the Minneapolis-St Paul, Minnesota, area between September 2006 and March 2011.

Patients were invited to participate in the study if they were receiving ventilatory support for acute respiratory failure, were alert, participating in their daily care routines, appropriately following commands, cognitively intact to participate in the consent process, and had adequate or corrected vision and hearing. Patients were not approached if they were receiving aggressive ventilatory support, requiring vasopressors, unresponsive or delirious, receiving chronic ventilator support prior to hospitalization, or had a documented mental incompetence (eg, Alzheimer disease).

The target sample size of 286 was based on power analysis calculations

that required 48 hours or longer of protocol data and allowed for 20% attrition. Other parameters were an α level of .05 and a power level of 80% based on a repeated-measures analysis of covariance, which provides a good approximation for mixed models. A prior study¹⁶ had a mean (SD) score of 50.5 (29.2) mm on the visual analog scale for anxiety (VAS-A; scale range: 0-100 mm). A difference of 15.2 mm or greater would be detected as a statistically significant difference among groups. For the sedative-exposure aim, previous data gave a mean (SD) estimate of 6.5 (4.3).¹⁷ Using the sample size determined for the VAS-A, any difference of 1.8 or greater in the sedation intensity would be detected as a statistically significant difference among groups.

Study approval was obtained from the University of Minnesota's institutional review board (IRB) and from the participating hospitals' IRBs. Given the patient-directed nature of the protocol, the IRB required patients to provide their own written informed consent. To validate patient understanding of the study's risks, benefits, and procedures, the patient had to answer 7 yes or no questions correctly to the research nurses. If any of the questions was answered incorrectly, that patient was not enrolled that day but remained eligible to be reapproached if mental status improved and inclusion criteria were still met. Trained research nurses obtained all written consents.

Data were obtained on sex, age, days mechanically ventilated, and days in the ICU prior to enrollment, diagnoses, ventilator settings, and all medications received 24 hours prior to enrollment. Data from each patient's ICU admission day were abstracted from the medical record to calculate the Acute Physiology, Age and Chronic Health Evaluation III (APACHE III) score, which was used as a covariate to control for illness severity.

Anxiety was defined as a state marked by apprehension, agitation, increased motor activity, arousal, and fearful withdrawal.¹⁸ Anxiety was assessed via self-

report at study entry and daily while ventilated using the 100-mm VAS-A, which was presented to patients with a vertical orientation like a thermometer. The bottom of the scale was anchored by the statement "not anxious at all" and the top was anchored by "most anxious ever." Patients indicated their current level of anxiety in response to "How are you feeling today?" The VAS-A score was the number of millimeters from the bottom edge of the line anchor to the patient's mark. The VAS-A and the Spielberger State Anxiety Inventory are correlated ($r=0.49$ ¹⁶ to $r=0.82$ ¹⁹), demonstrating concurrent validity.

Sedative exposure was determined for all patients who received any of 8 commonly administered sedative and analgesic medications in the ICU (midazolam, lorazepam, propofol, dexmedetomidine, morphine, fentanyl, hydromorphone, haloperidol) 24 hours prior to enrollment and each day during the study. Sedative exposure was operationalized as a daily sedative drug intensity score and sedative dose frequency.¹⁷ The usual practice at the participating ICUs consisted of physicians writing orders for sedation therapy per their individual preferences with the nurses managing administration of these medications within the parameters of the orders. Sedative administration was not directed by a specific unit protocol or by a study protocol.

The sedative drug intensity score aggregated dose amounts of medications from disparate drug classes by using a weight-adjusted dose (adjusting for differing patient weights) of each sedative administered during 4-hour time blocks during mechanical ventilation. Every drug amount (eg, 2 mg of lorazepam administered between noon and 4 PM) was then placed into quartiles created by using all patients' lorazepam data during the entire time they received the study protocol; 2 mg of lorazepam might fall into quartile 2. If fentanyl also was given at a dose that fell into quartile 3 for all fentanyl doses within the entire sample, then the noon-4 PM value was 5 (2 + 3). If none

of the 8 medications was given, the value was 0. The values were summed over the six 4-hour blocks to produce a daily sedative drug intensity score. For dose frequency, a 24-hour day was divided into six 4-hour time blocks and, for each of the 8 drugs, the occurrences in which a sedative was administered at least once during that interval were summed. This approach to sedative exposure accounts for medications administered to patients from nonequivalent, disparate drug classes.¹⁷

The environmental scan form was developed for this study to collect data on the overall activity level in the patient's room each shift and on ICU nursing experience. Nurses were invited to provide any comments about the study protocol. This paper and pencil form was adhered to a brightly colored clipboard kept at each participant's bed side.

A starter set of 6 CDs were reviewed with the patient by the research nurse to provide for immediate listening upon randomization to the PDM group. The starter set included relaxing music played on piano, harp, guitar, and Native American flute. The research nurse oriented the patient to CD player and headphone operation. A standard CD/MP3 player with comfortable, noise-abating headphones was kept within easy reach to allow the patient to self-initiate music listening.

Within 24 hours of randomization, the music therapist completed a music preference assessment on each PDM patient using a tool designed to assess music preferences of mechanically ventilated patients with a simple yes or no format.²⁰ Patients were prompted verbally and with posted signs to use music at least twice per day when feeling anxious and/or to provide relaxation, but were encouraged to self-initiate music listening as frequently as desired. Nursing staff were encouraged to offer music at least twice during their shift, but were reminded by the research staff that the decision to listen was determined by the patient. A data-logger system on the headphones captured each PDM session and total daily music listening time; system details are described elsewhere.²¹

Patients randomized to the active control NCH group were encouraged to wear headphones whenever they wanted to block out ICU noise or have some quiet time. As with the PDM group, NCH patients self-initiated headphone use. Patients randomized to the usual care control group received standard ICU care for that respective unit. Patients had daily assessment visits by a research nurse who administered the VAS-A. Patients remained on protocol up to 30 days as long as they were receiving ventilatory support.

Descriptive statistics and graphing were performed on all study data to assess the distributions of the variables. We used bivariate associations to identify covariates to be considered in subsequent analyses. Covariates were not included to assess their effect per se or to adjust for imbalance among groups, but were included if significantly associated with the outcome to subtract the variability piece they represent and thus gain efficiency.

Patients with at least 2 days of VAS-A scores and sedative exposure data were used in the change over time analyses. Change over time was assessed as the slope of the outcome variables determined from one day to the next using the best fitting line. We used mixed-effects models to analyze anxiety and sedative exposure (sedation intensity scores and sedation frequency) because they accommodate measures that are correlated from one time point to another and have variances that are not constant from one time point to another, which would be expected in a repeated-measures analysis of covariance. This is the recommended modeling for intent-to-treat analyses.²² Using the data as is within a mixed-model analysis has a lower type I error and higher power than any type of imputation method used for missing data, which would be needed for a repeated-measures analysis of covariance. Also, imputation may result in biased estimates of effects and standard errors. A series of models were estimated and compared with the Aikake information criterion and the Bayesian infor-

mation criterion to determine the best model of change for the anxiety and sedative exposure data.

An unconditional means model was used to assess 2 null hypotheses: no change across occasions; and no variation among patients. Rejecting these null hypotheses warrants further analysis. An unconditional growth model with day added as a predictor incorporated estimation of change coefficients. Models with several within-person error covariance structures that were compatible with the correlation pattern between anxiety measures and sedative exposure measures at different time points were explored. The best fit was the autoregressive plus random-effects covariance structure that assumes correlations decrease as the lag time increases and that covariance also comes from measures within subject. An unconditional growth model with a quadratic term was also explored to assess if there were nonlinear changes in sedative exposure measures over time.

A conditional growth model introduced the effect of the intervention and included any covariates found to be associated with the outcome. These were included in the analysis to eliminate the variability attached to them and improve the precision of the β estimates. Post hoc multiple comparisons were completed within the mixed modeling controlling the overall α level at .05. We used SPSS version 17 (SPSS Inc) and SAS version 9.2 (SAS Institute Inc) statistical software. Final parameter estimates were considered significant at a P value of .05 or less with a 2-sided α .

RESULTS

TABLE 1 summarizes the characteristics of the patients. The mean age was 59 years with a wide range of APACHE III scores. The primary indication for mechanical ventilation was respiratory failure or distress. Only median ICU days prior to enrollment were significantly different at study entry; NCH patients were in the ICU 1 to 2 days longer prior to enrollment than PDM or usual care patients. Patients remained on protocol for a mean (SD) of 5.7 (6.4)

days (median, 3.2 [range 1-30] days). FIGURE 1 details patient flow through the study.

The PDM patients listened to music for a mean (SD) of 79.8 (126) minutes/day (median, 12 [range, 0-796] minutes/day). The NCH patients wore the noise-abating units for a mean (SD) of

34.0 (89.6) minutes/day (median, 0 [range, 0-916] minutes/day). There was no linear relationship between device use time and anxiety for either the PDM group ($r=0.07$; $P=.14$) or the NCH group ($r=-0.06$; $P=.23$). More PDM patients were extubated at the end of the study (Table 1).

The analysis is from the 241 patients with 2 or more anxiety assessments in order to model change. Not all patients were able to provide anxiety assessments each day due to fatigue, medical condition, state of sedation, inability or refusal to complete assessments, or were off the unit (Figure 1). Unadjusted mean VAS-A score was not significantly different among groups at study entry (Table 1). We did not observe a nonlinear pattern or any obvious inflection point in the individual patterns of change; therefore, change was modeled as linear. Both the unconditional means model and the unconditional growth model indicated significant unexplained variance that warranted further modeling. Covariates of interest in the model were scores on the APACHE III and VAS-A at enrollment and sedative exposure.

Two final models were produced using either sedation frequency or sedation intensity (TABLE 2). After the adjustment due to APACHE III and sedation frequency and intensity, the adjusted baseline VAS-A score was different among study groups, and the interaction of baseline with treatment group was significant. Pairwise comparisons indicated that PDM patients had a significantly lower VAS-A score at study entry than usual care patients, regardless of whether sedation intensity or frequency was used. Sedation intensity ($\beta=0.75$ [95% CI, 0.01 to 1.50]; $P=.05$) was associated with higher VAS-A scores. After adjusting for these covariates, the final models showed that the main effect of PDM was to lower VAS-A scores consistently by more than 19 mm during the study period compared with usual care (sedation intensity: $\beta=-19.3$ [95% CI, -32 to -6.6]; and sedation frequency: $\beta=-19.5$ [95% CI, -32.2 to -6.8]; $P=.003$ for both) (FIGURE 2).

The analysis is from the 266 patients who were on protocol for 48 hours or longer. A linear pattern of change was supported by graphs of sedation intensity and frequency over time. Sedation frequency and intensity were not significantly different

Table 1. Demographic and Clinical Characteristics of Patients (N = 373)

	Patient-Directed Music (n = 126)	Noise-Canceling Headphones (n = 122)	Usual Care (n = 125)	P Value
Age, mean (SD), y	60.4 (15.4)	59.4 (14.3)	57.8 (13.5)	.37
Female sex, No. (%)	68 (54)	56 (46)	69 (55)	.28
APACHE III score, mean (SD)	63.1 (18.7)	62.2 (22.3)	65.6 (23.5)	.43
Length of ICU stay prior to study entry, median (range), d	6 (0-40)	8 (1-85)	7 (0-33)	.02
Ventilator use, median (range), d				
Prior to study entry	4.5 (0-35)	6.0 (1-79)	6.0 (0-38)	.11
Prior to study entry + study days	7.5 (1-53)	7.3 (1-47)	7.7 (1-46)	.74
Enrolled per protocol, median (range), d	3.0 (1-27)	3.6 (1-30)	3.8 (1-30)	.66
VAS-A score at study entry, mean (SD), mm	51.9 (32.4)	49.0 (30.1)	52.3 (29.7)	.66
Sedation 24 h prior to enrollment, median (range)				
Intensity score	4.0 (0-12)	3.5 (0-10)	4.0 (0-12)	.07
Frequency	7.0 (0-18)	6.0 (0-19)	6.0 (0-14)	.14
Extubated at end of study, No. (%)	89 (71)	67 (55)	83 (66)	.02
Alive at end of study, No. (%)	115 (91)	111 (91)	109 (87)	.65
Primary ICU admission diagnosis category, No. (%)				
Pulmonary	77 (61)	70 (57)	71 (57)	
Cardiac				
Medical	14 (11)	9 (7)	9 (7)	
Surgical	0	3 (2)	3 (2)	
Sepsis or infection	10 (8)	7 (6)	6 (5)	
Gastrointestinal	6 (5)	8 (7)	7 (6)	
Neurological or neuromuscular	2 (2)	6 (5)	7 (6)	
Oncology	4 (3)	3 (2)	4 (3)	
Shock or hypotension	3 (2)	2 (2)	5 (4)	
Trauma	3 (2)	4 (3)	2 (2)	
Surgical	2 (2)	3 (2)	0	
Vascular	2 (2)	0	2 (2)	
Other or missing	3 (2)	7 (6)	9 (7)	
Indication for mechanical ventilation, No. (%)				
Respiratory failure	63 (50)	63 (52)	61 (49)	
Respiratory distress	32 (25)	27 (22)	36 (29)	
Pneumonia	7 (6)	5 (4)	7 (6)	
Respiratory arrest	3 (2)	4 (3)	4 (3)	
Airway protection	2 (1)	5 (4)	4 (3)	
Surgery or postoperative	2 (1)	3 (2)	4 (3)	
COPD	7 (6)	4 (3)	0	
Hypoxia	2 (1)	3 (2)	2 (2)	
ARDS	1 (1)	1 (1)	0	
Tachypnea	1 (1)	0	1 (1)	
Cardiac arrest	4 (3)	2 (2)	5 (4)	
Pulmonary edema	1 (1)	0	0	
Asthma	0	0	1 (1)	
Other or missing	1 (1)	5 (4)	0	

Abbreviations: APACHE III, Acute Physiology, Age and Chronic Health Evaluation III; ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; VAS-A, visual analog scale for anxiety.

among groups 24 hours prior to study entry (Table 1).

Covariates associated with sedation intensity and sedation frequency were age, sex, and APACHE III scores. Age was significant in both models; the higher the age, the lower the sedation intensity or sedation frequency. In the models, there was a significant interaction between the PDM group and time, which showed a decrease in sedation intensity and sedation frequency over time (per day) for the PDM group only (Table 2). In post hoc pairwise comparisons, the PDM group had a greater decrease in the change over time of the sedation intensity score compared with the usual care group ($\beta = -0.18$ [95% CI, -0.36 to -0.004];

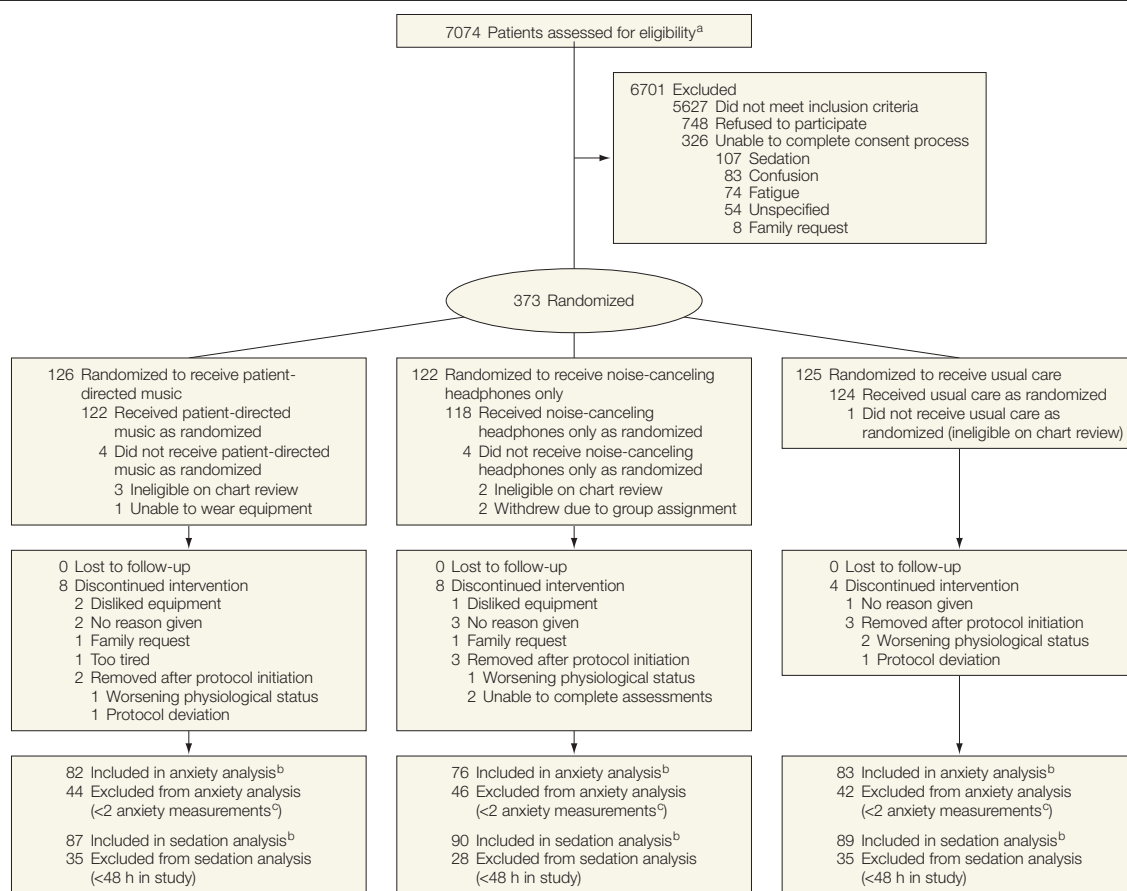
$P = .05$). Using the sedation frequency measure, the PDM group had a greater decrease in the change over time compared with the usual care group ($\beta = -0.21$ [95% CI, -0.37 to -0.05]; $P = .01$) and the NCH group ($\beta = -0.18$ [95% CI, -0.36 to -0.004]; $P = .04$) (FIGURE 3 and FIGURE 4).

For an average patient on the fifth study day (the average time patients were enrolled), a usual care patient received 5 doses of any 1 of the 8 study-defined sedative medications. An equivalent PDM patient received just 3 doses on the fifth day, a relative reduction of 38%. By the end of the fifth day, an average usual care patient had a sedation intensity score of 4.4. An equivalent PDM patient had a sedation inten-

sity score of 2.8, a relative reduction of 36%. By the end of the fifth day, an average usual care patient had an anxiety score of 52. An equivalent PDM patient had an anxiety score of 33, which is an absolute difference of 19 on a 100-point scale and a relative reduction of 36.5% (TABLE 3).

Nurses caring for patients had a median of 5.9 years (range, 0.25-44 years) of ICU experience. When asked to appraise the shift activity in the patient's room, 21% of the nurses said quiet, 49% said it was at a usual pace, 24% said it was busy, 6% said it was very busy to hectic. Comments included the nurses' efforts offering PDM or headphones to patients and their observations of the protocol (BOX).

Figure 1. Flow Diagram of Study



^aThis number is an estimate based on the number of days patients were mechanically ventilated, screened, and had confirmed pulmonary diagnosis.

^bThose who withdrew or were removed after completing at least 48 hours in the study were included in the analysis.

^cThe reasons why anxiety assessment was not completed included sedated, sleeping, off unit, too tired, and unable to respond to questions.

DISCUSSION

The 2 primary study aims were to determine if PDM reduced anxiety and sedative exposure in a sample of patients receiving mechanical ventilatory support. The PDM intervention decreased anxiety and sedative exposure over time more effectively than usual care or NCH. To our knowledge, these findings are from the first randomized clinical trial to test an integrative

therapy for self-management of anxiety in ventilated ICU patients that does not rely solely on medications. The unique approach involving patients themselves in self-management of anxiety launches a novel area of ICU clinical research.

The PDM protocol was modeled after the patient-controlled analgesia intervention whereby patients report better pain control and are more satisfied

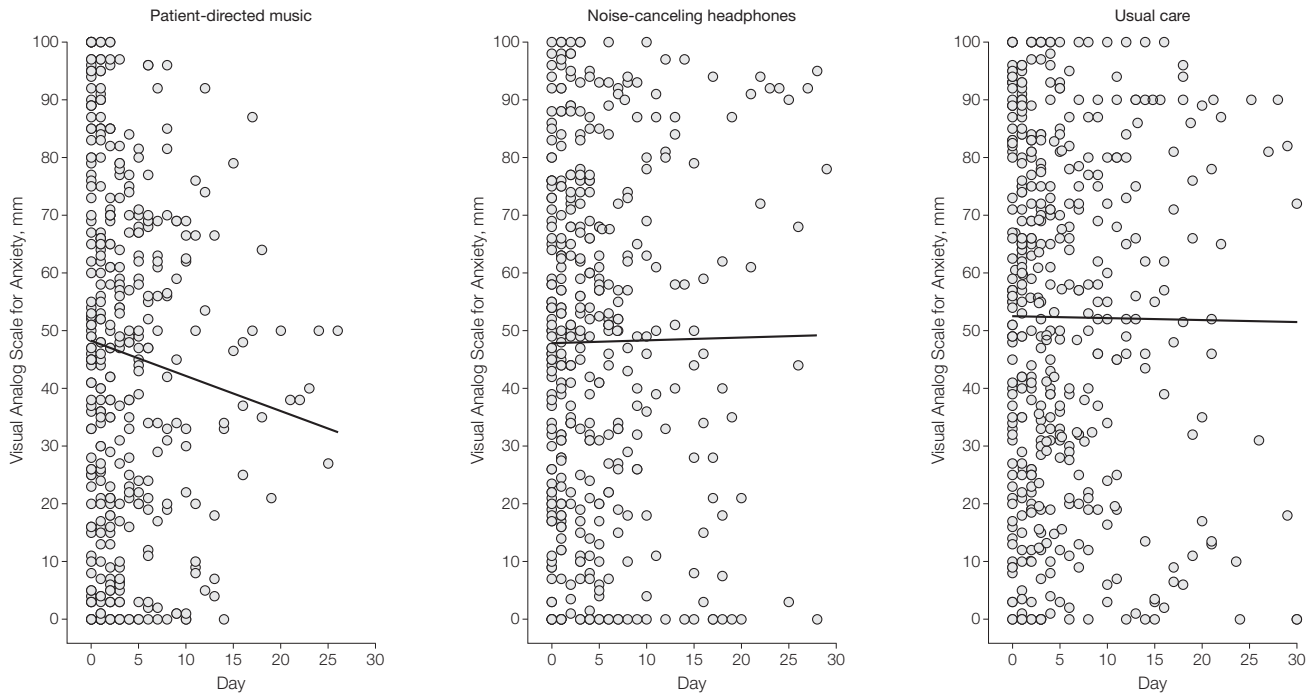
when they self-administer analgesic therapy.^{8,23,24} Music provides patients with a comforting and familiar stimulus and the PDM intervention empowers patients in their own anxiety management; it is an inexpensive, easily implemented nonpharmacological intervention that can reduce anxiety, reduce sedative medication exposure, and potentially associated adverse effects.²⁵⁻²⁹ The PDM patients received less

Table 2. Final Models for Anxiety and Sedative Exposure Based on 2 or More Days of Data^a

	Model Results for VAS-A (n = 241)				Model Results for Sedation (n = 266)			
	Sedation Frequency		Sedation Intensity		Intensity		Frequency	
	β (95% CI) ^b	P Value	β (95% CI) ^b	P Value	β (95% CI) ^c	P Value	β (95% CI) ^d	P Value
Intercept ^e	35.6 (23.3 to 48.0)	<.001	34.9 (22.6 to 47.2)	<.001	5.3 (3.5 to 7.1)	<.001	7.3 (5.1 to 9.5)	<.001
Day	-0.50 (-1.10 to 0.05)	.08	-0.51 (-1.10 to 0.04)	.07	-0.03 (-0.15 to 0.09)	.65	-0.17 (-0.27 to -0.07)	<.001
VAS-A score at day 0	0.11 (-0.05 to 0.27)	.18	0.11 (-0.05 to 0.27)	.18				
Patient-directed music	-19.5 (-32.2 to -6.8)	.003	-19.3 (-32.0 to -6.6)	.003	0.14 (-0.92 to 1.20)	.79	0.69 (-0.68 to 2.10)	.33
Noise-canceling headphones	-8.3 (-21.4 to 4.8)	.22	-8.3 (-8.7 to -7.9)	.21	0.18 (-0.86 to 1.20)	.73	-0.01 (-1.30 to 1.30)	.99
APACHE III score	0.16 (0.02 to 0.30)	.02	0.16 (0.02 to 0.30)	.02	0.003 (-0.01 to 0.02)	.79	0.005 (-0.01 to 0.02)	.65
Age					-0.03 (-0.05 to -0.01)	.03	-0.04 (-0.08 to -0.008)	.03
Sex					0.88 (0.15 to 1.60)	.02	0.94 (0.02 to 1.90)	.047
Patient-directed music × day					-0.18 (-0.36 to -0.004)	.05	-0.21 (-0.37 to -0.05)	.01
Noise-canceling headphones × day					-0.08 (-0.24 to 0.08)	.32	-0.03 (-0.17 to 0.11)	.72
Adjusted sedation Intensity			0.75 (0.01 to 1.50)	.05				
Frequency	0.42 (-0.15 to 0.99)	.14						
VAS-A score at day 0 × Patient-directed music	0.25 (0.03 to 0.47)	.02	0.25 (0.03 to 0.47)	.02				
Noise-canceling headphones	0.11 (-0.13 to 0.35)	.33	0.12 (-0.12 to 0.36)	.32				
Pairwise comparisons ^f								
Patient-directed music vs noise-canceling headphones	0.14 (-0.08 to 0.36)	.24	0.13 (-0.09 to 0.35)	.24	-0.09 (-0.27 to 0.09)	.32	-0.18 (-0.36 to -0.004)	.04
Patient-directed music vs usual care	0.25 (0.03 to 0.47)	.02	0.25 (0.03 to 0.47)	.02	-0.18 (-0.36 to -0.004)	.05	-0.21 (-0.37 to -0.05)	.01
Noise-canceling headphones vs usual care	0.11 (-0.13 to 0.35)	.33	0.12 (-0.12 to 0.36)	.32	-0.08 (-0.24 to 0.08)	.32	-0.03 (-0.17 to 0.11)	.72

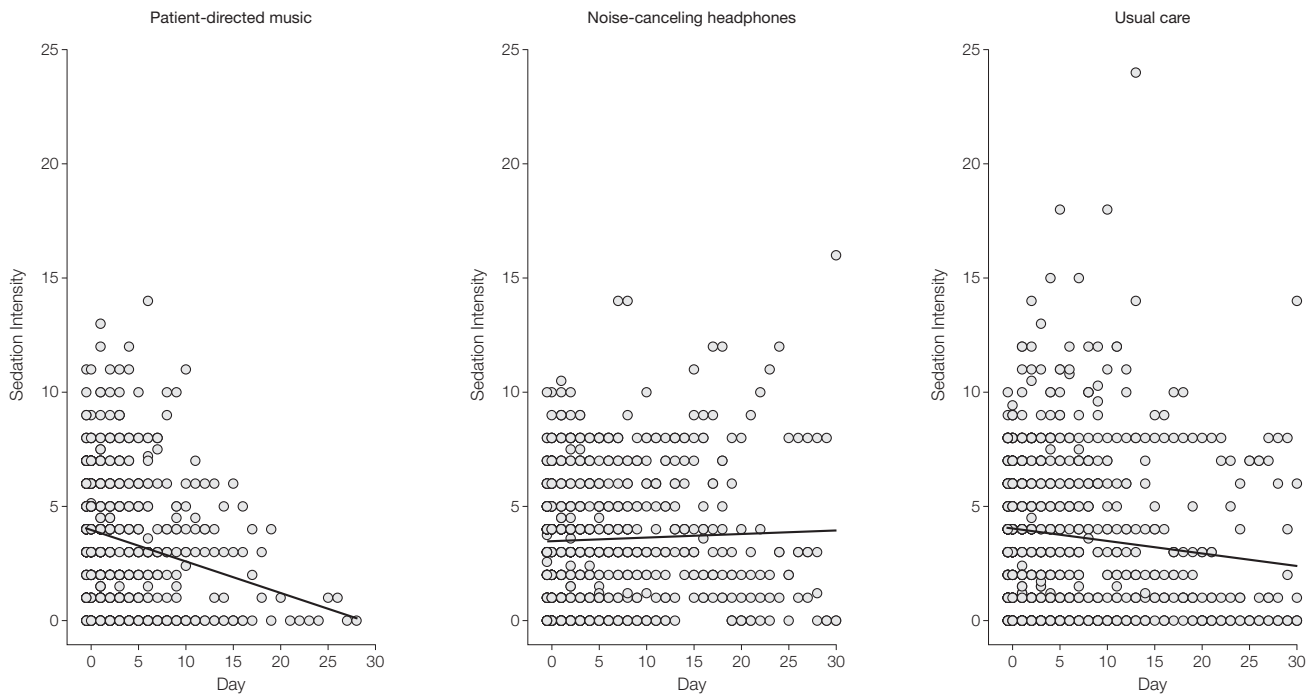
Abbreviations: APACHE III, Acute Physiology, Age and Chronic Health Evaluation III; VAS-A, visual analog scale for anxiety.
^aThe following sentence is an example of how to interpret this table. The formula to predict sedation frequency for the patient-directed music group at any time point: sedation frequency = 7.3 minus 0.17 (day in study) minus 0.21 (day if in the patient-directed music group) plus 0.69 (if in the patient-directed music group) plus 0.005 (APACHE III score) minus 0.04 (age) plus 0.94 (if female).
^bIndicates change in millimeters for VAS-A for 1 unit change in predictor.
^cIndicates change in sedation intensity for 1 unit change in predictor.
^dIndicates change in sedation frequency for 1 unit change in predictor.
^eRepresents the overall average of frequency sedation at baseline (7.3 doses). Each patient's dose decreased by an average of 0.17 doses per day. If the patient was in the patient-directed music group, for each day, the dose frequency decreases by another 0.21 points per day (0.17 + 0.21 = 0.38). If the patient was in the patient-directed music group, the baseline average was 0.69 higher (7.30 + 0.69 = 7.99), every increase of 1 point in the APACHE III score raises the total daily dose frequency by another 0.005. For every 1 year older a patient was, his/her sedation frequency decreased by 0.04 points. If the patient was female, the dose frequency increased by 0.94.
^fThe data in columns 2 through 5 are for VAS-A scores at day 0.

Figure 2. Visual Analog Scale for Anxiety Scatterplots by Group



The diagonal and horizontal lines are the best fitted lines to demonstrate change over the study period.

Figure 3. Sedation Intensity Scatterplots by Group



The diagonal and horizontal lines are the best fitted lines to demonstrate change over the study period.

frequent and less intense sedative regimens while reporting decreased anxiety levels.

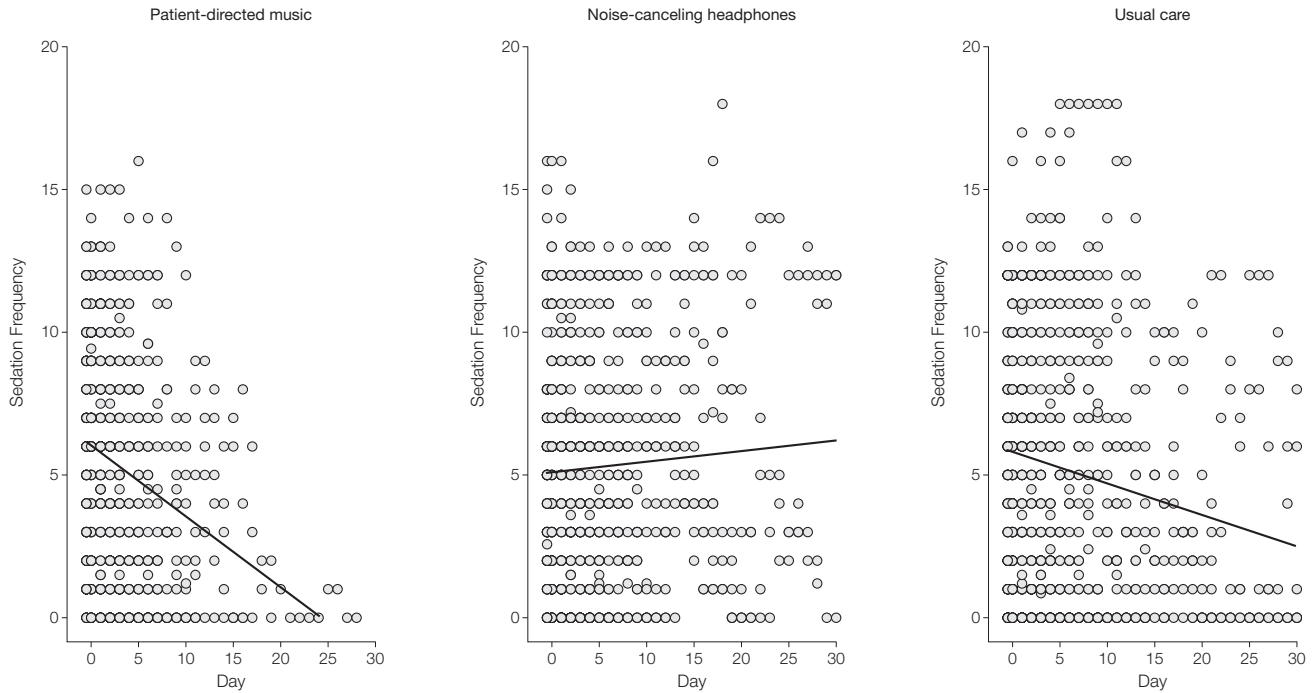
We report a reduction in sedative exposure with PDM using a method to aggregate medications from disparate drug

classes. This is a significant finding in that strategies are needed to reduce the amount and frequency sedative medications are administered to mechanically ventilated ICU patients. An appropriately tailored music intervention holds great

promise for use in clinical practice as a method to potentially avoid or reduce the cumulative adverse effects of these potent medications, but requires further study.

As more clinicians are advocating to minimize sedative administration,^{30,31}

Figure 4. Sedation Frequency Scatterplots by Group



The diagonal lines are the best fitted lines to demonstrate change over the study period.

Table 3. Visual Analog Scale for Anxiety (VAS-A) and Sedative Exposure Using Mixed-Effects Models^a

	APACHE III Score	Sedation Score		Baseline VAS-A Score, mm	Estimated VAS-A Score, mm					
		Intensity	Frequency		Using Sedation Intensity ^b			Using Sedation Frequency ^c		
					Patient-Directed Music	Noise-Canceling Headphones	Usual Care	Patient-Directed Music	Noise-Canceling Headphones	Usual Care
Median score	64	4	7	52	33	44	52	32	43	51
	APACHE III Score	Sedation Score		Female sex	Estimated Sedation Measures					
		Intensity ^d	Frequency ^e		Intensity ^d			Frequency ^e		
Median score	64			4	7		2.8	4.2	4.4	3.3

Abbreviation: APACHE III, Acute Physiology, Age and Chronic Health Evaluation III.

^aSedative exposure defined as the dose frequency and the sedation intensity. Patient age of 60 years, APACHE III scores, and study day 5 kept constant throughout model.

^bIt would be estimated that the usual care group would have an anxiety rating of 52 mm at 5 days into the study. For the noise-canceling headphones group, they would have an anxiety rating of 44 mm, a decrease of 8 points (in millimeters). For the patient-directed music group, they would have an anxiety rating of 33 mm, a decrease of 19 mm from usual care at 5 days into the study. By day 5, patient-directed music reduces VAS-A score by 37% compared with usual care.

^cThe usual care group would have an anxiety rating of 51 mm at 5 days into the study. The noise-canceling headphones group would have an anxiety rating of 43 mm, a decrease of 8 points (in millimeters). The patient-directed music group would have an anxiety rating of 32 mm, a decrease of 19 mm from usual care. By day 5, patient-directed music reduces VAS-A score by 37% compared with usual care.

^dIndicates the sum of the dose quartiles over 8 medications. For an average patient with usual care, his/her sedation intensity score would be 4.4 at 5 days into the study. The noise-canceling headphones group would be 4.2, a decrease of 0.2. The patient-directed music group would be 2.8, a decrease of 1.6 from usual care. By day 5, patient-directed music reduces sedation intensity by 36% compared with usual care.

^eFor an average patient in usual care, his/her sedation frequency score would be 5.3 at 5 days into the study. The noise-canceling headphones group would be 5.2, a decrease of 0.1. The patient-directed music group would be 3.3, a decrease of 2.0 from usual care at 5 days. By day 5, patient-directed music reduces sedation frequency by 38% compared with usual care.

our data suggest that patients still experience moderate levels of anxiety. Patients in this study with higher sedation intensity scores had higher VAS-A scores. This finding is consistent with previous investigations that demonstrate ICU patients report moderate anxiety levels throughout the course of ventilatory support, despite receiving sedative medications.⁷ Given the detrimental physiological and psychological effects of sustained anxiety, it is important that this symptom be effectively managed. As clinicians seek lighter sedative regimens in the ICU, PDM may be an appropriate adjunctive intervention by which patients can self-manage anxiety. There were no comments from nurses that would suggest the study protocol was burdensome to their patient care practices.

Because patients were enrolled when they were not receiving high levels of sedative medications (otherwise they would have been too sedated to provide consent at enrollment), it is difficult to interpret the pharmacological or cost significance of a reduction in sedative exposure in the days after enrollment compared with the higher doses patients likely received earlier in their episode of respiratory failure. However, even with a modest reduction in sedative exposure, patients assigned to PDM also experienced less anxiety compared with usual care.

There are a number of limitations to this study. Because research nurses completed the anxiety assessments (to ensure consistent administration and minimize influence on the bedside nurse's practice), only 1 anxiety assessment was performed daily. For some patients, the assessment was not performed in relation to use of the PDM intervention, and if the patient was not available or the patient deferred due to fatigue, medical condition, or was sedated, the assessment was not completed (Figure 1).

Because the intervention was initiated by the patient, not all those randomized to PDM actually used music twice daily. Some patients may have re-

Box. Summary of Intensive Care Unit Nurse Written Comments and Observations

Patient-directed music group

Patient's wife says he listens to the music all of the time and it has been working well. Patient was sleeping with headphones on with his wife sleeping next to him in a chair.

Patient looks very peaceful and states she likes the music.

Patient was tapping fingers to some of the music provided to him by the music therapist.

Patient listened to music most of yesterday (about 10 h). Tends to be anxious and her blood pressure is lower when she is listening to music.

Patient likes music and always nods head "yes" to have headphones in place when asked.

After putting headphones on, patient appears less anxious.

Patient wears headphones very often and rests well with them in place. Always nods "yes" to wearing headphones.

Patient has been tapping feet to the music and listens for a couple of hours each night; seems happy with it!

After putting headphones on, patient appears less anxious.

Able to decrease propofol slightly.

Evening was quieter. Patient put headset on which seemed to help a lot.

Family visited for 1 h. Patient had difficulty sleeping; tried reading and quiet time before using headphones.

Patient calm and resting with headphones on.

Patient was relaxing with music on for 3 h.

Patient slept well, headphones for 3 h.

Music was on entire night (8-h shift).

Noise-canceling headphones group

Patient really benefited from headphones!

Patient relaxed with headphones.

I'm glad he's participating. I think the headphones will help him rest.

The headphones would help her get more rest (due to the commotion on the other side of the curtain with roommate).

The patient wanted to wear the headphones most of the day yesterday and communicated that they helped her rest.

Patient put headphones on without prompting.

Headphones helped patient sleep during dialysis.

Patient wanted to wear headphones all night.

Patient had earphones on about 1 h early in the night, then declined to use them the rest of night.

Headphones decrease nerves (per patient and patient's wife).

Patient appeared calmer with headphones on.

lied on the bedside nurse to assist with the equipment. This may have affected the length or frequency of music listening by patients or the nonsignificant relationship between music

listening time and anxiety. However, simply having the option and availability of PDM may provide patients a sense of control over one aspect of their ICU care. Given that anxiety is an

individually perceived symptom, self-initiation of treatment with music whenever desired and for as long as desired is the preferred method of music listening much in the same manner as patient-controlled analgesia for pain relief.

Only a small number of nurses provided written comments about the protocol. While positive, it is unknown if the ICU nurses were reluctant to record negative comments, despite the comments being anonymous. We did not query nurses for the reasons why they administered sedative medications to study patients. The ICU nurses were not blinded to assignment group, which may have introduced bias into the study. Furthermore, we did not collect data from patients after they were extubated or transferred from the ICU.

CONCLUSIONS

Among ICU patients receiving acute ventilatory support for respiratory failure, PDM resulted in greater reduc-

tion in anxiety compared with usual care, but not compared with NCH. Concurrently, PDM resulted in greater reduction in sedation frequency compared with usual care or NCH, and greater reduction in sedation intensity compared with usual care, but not compared with NCH.

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Study concept and design: Chlan, Weinert, Skaar, Savik. **Acquisition of data:** Chlan, Guttormson.

Analysis and interpretation of data: Chlan, Weinert, Heiderscheit, Tracy, Skaar, Guttormson, Savik.

Drafting of the manuscript: Chlan, Heiderscheit, Skaar, Savik.

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Statistical analysis: Heiderscheit, Savik.

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