

## Original Article

# Effects of traditional music therapy on the psycho-neuro-immuno-endocrine aspect of burnout syndrome in healthcare workers: A randomized controlled trial

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## Abstract

Burnout syndrome (BOS) is an occupational phenomenon highly prevalent among healthcare workers, particularly physicians and nurses. Despite its prevalence, no single therapy universally addresses all cases of BOS. The aim of this study was to develop a novel approach to managing BOS through traditional music therapy, evaluated from psychosomatic, neurological, immunological, and endocrine perspectives. The study involved 80 participants who were randomly assigned to either the intervention or control group. The intervention group received traditional music therapy for 10–15 minutes, three times a week, over four weeks. Key outcomes were assessed at weeks 2 and 4. Measurements included the Maslach Burnout Inventory (MBI), heart rate variability (HRV), saliva cortisol, saliva  $\beta$ -endorphin, saliva immunoglobulin A (IgA), and serum FOXP3. Instruments included the MBI-HSS questionnaire and HRV measuring devices. Over four weeks, significant improvements were observed in the MBI scores ( $p=0.001$ ), HRV ( $p=0.001$ ), and FOXP3 delta ( $p=0.035$ ) in the intervention group compared to the control group. However, no significant differences were found for cortisol,  $\beta$ -endorphin, or IgA. These findings suggest that traditional music therapy positively impacts the psychological, neurological, and immunological aspects of BOS and potentially influences immunological and endocrine responses. Future research should explore the effects of longer intervention durations, test varying doses, and examine the combination of music therapy with other non-pharmacological treatments to enhance its therapeutic potential.

**Keywords:** Traditional music, music therapy, burnout, burnout syndrome, healthcare workers

## Introduction

Burnout syndrome (BOS), initially described by Freudenberg in the 1970s, has become recognized worldwide as a distinct occupational phenomenon. It is characterized by a response to persistent workplace stress, manifesting in three dimensions: emotional exhaustion,



depersonalization, and reduced personal accomplishment [1,2], according to the Maslach Burnout Inventory (MBI), which remains the primary diagnostic tool for assessing these aspects of burnout [3].

High-stress professionals, particularly healthcare workers, frequently experience burnout due to constant psychological and physical demands, leading to impaired function and reduced productivity [4]. A study on healthcare providers showed that burnout correlated with decreased patient care quality, heightened costs, and increased absenteeism [5]. These impacts arose from lower productivity and overall health deterioration among affected workers [5]. However, despite its high prevalence, a universally standardized therapy for BOS is still lacking, due to its complex, multifactorial nature and the variability in populations affected by it [6].

Neurophysiological aspects of burnout can be evaluated using heart rate variability (HRV), which measures fluctuations between consecutive heartbeats, reflecting autonomic nervous system activity. HRV, divided into time and frequency domains, provides insight into sympathetic and parasympathetic balance [7], where high HRV typically signals greater stress adaptability [8]. Additionally, the hypothalamic-pituitary-adrenal (HPA) axis plays a central role in modulating immune responses during stress, influencing cytokine production and regulatory T cell function [9]. Dysregulation in BOS patients often involves T cell suppression, as indicated by biomarkers such as forkhead box P3 (FOXP3) [10], and immunoglobulin A (IgA), both of which are closely linked to stress response [11,12]. While cortisol is a valuable indicator of acute stress response, its effectiveness in gauging chronic stress remains inconclusive [13-18].  $\beta$ -endorphin, a neurochemical connected to stress regulation, exhibits lower plasma concentrations in individuals with chronic stress conditions like post-traumatic stress disorder (PTSD), linking it to hyperarousal and anxiety [19].

Music therapy has emerged as a non-pharmacological intervention aimed at addressing physical, emotional, and cognitive facets of stress [20]. It stimulates brain regions like the amygdala and hypothalamus, both integral to stress modulation [21]. Traditional music in Indonesia, as a culturally resonant therapy, has been noted to enhance therapeutic experiences by fostering a strong emotional connection, thereby reinforcing its potential as an alternative BOS management approach [22]. The aim of this study was to investigate the efficacy of traditional music therapy in managing burnout among healthcare workers, with evaluations focused on psychological, neurological, immunological, and endocrine responses.

## Methods

### Study design and setting

A randomized controlled trial was conducted at Dr. Kariadi General Hospital, Semarang, Indonesia, from January to June of 2024. It used a pre- and post-test control group design with cluster random allocation. The health workers with moderate to severe BOS were randomly assigned to intervention and control groups, with the intervention group receiving music therapy and psychoeducation for four weeks. The outcomes (psychological, neurological, immunologic, and endocrine responses) were assessed prior to intervention and at week 2 and week 4 after the intervention.

### Participants and criteria

The inclusion criteria were health workers at Dr. Kariadi Hospital, aged between 18 and 60 years, with a Maslach Burnout Inventory-Human Services Survey (MBI-HSS) score above 44 which indicates moderate to severe BOS, and employed in their current department for at least one year. Participants were excluded if they had hearing impairments, chronic conditions (e.g., cancer, thyroid disease, heart disease, uncontrolled diabetes, or hypertension), mental health disorders which were screened using Mini-International Neuropsychiatric Interview (MINI) ICD-10, pregnancy, regular use of central nervous system-altering medications, or a stated dislike of music. Dropout criteria for this study were if participants were unable to complete the study.

### Intervention

Cluster random sampling was employed to allocate respondents into two distinct groups: (1) the intervention group, which received music therapy and psychoeducation; and (2) the control

group, which received psychoeducation related to BOS only. The intervention consisted of music therapy sessions delivered via standardized listening techniques, equipment, and structured timing. Each participant in the intervention group was provided with headphones containing a selection of culturally relevant, pre-arranged Indonesian songs with therapeutic attributes, emphasizing soothing melodies and soft instrumentation.

Music therapy sessions were conducted remotely, with participants using headphones at home while monitored through the Zoom application (Zoom Communications, Inc., San Jose, USA). The intervention was scheduled for 8:00 PM, with each session lasting 10–15 minutes. This duration was chosen based on expert recommendations to ensure relaxation without loss of engagement; sessions longer than 15 minutes could lead to fatigue, while shorter sessions sustain focus and therapeutic impact [23]. This music therapy was implemented three times weekly over a four-week period, balancing therapeutic exposure with practical integration into participants' schedules.

Psychoeducation was given in the form of educational videos about burnout syndrome. Educational videos were watched by the intervention group and the control group once at the beginning of the study. Educational videos were accessible during the four-week intervention period.

### Data collection

Baseline data collection (pretest) was conducted in week 0, with two follow-up assessments in the second and fourth weeks for all outcomes (psychological, neurological, immunologic, and endocrine responses). Psychological aspect was measured using the MBI-HSS tool and represented by MBI-HSS scores. MBI-HSS was specifically designed to evaluate the three aspects of burnout and is commonly utilized as a standard instrument for measuring BOS. The assessment focuses on three key dimensions: (1) emotional exhaustion, (2) depersonalization, and (3) a sense of low personal accomplishment. The tool consists of 22 questions, and answers were presented on a Likert scale ranging from 0, meaning "Never," to 6, meaning "Always." A score above 44 indicates a moderate to severe BOS.

HRV was measured using the Max Pulse portable HRV device (Medicore, Gyeonggi-do, South Korea). The device was placed on a stable surface to minimize movement during assessments. Each HRV evaluation included a 2-minute 30-second stress test and a 30-second vascular health test. Participants were instructed to keep their eyes open and refrain from moving or speaking during the assessment. If a participant had recently engaged in physical activity, a 10-minute rest period was required before measurement. Participants were also instructed to breathe normally without deep breathing during the procedure.

Blood and saliva samples were collected for biochemical analysis. The blood sample was collected using a 3 mL syringe, which was divided into two tubes: one with ethylenediaminetetraacetic acid (EDTA) anticoagulant for hematology analysis and one without anticoagulant for enzyme-linked immunosorbent assay (ELISA). The saliva sample was collected using a suction method that allowed saliva to accumulate in the oral cavity for 30 seconds. The collected saliva was transferred into a tightly sealed plastic storage tube using a 0.5 mL volume pipette and sent to Universitas Diponegoro's GAKI laboratory and Universitas Gajah Mada's Clinical Pathology Lab for analysis. GAKI laboratory tested saliva cortisol, saliva  $\beta$ -endorphin, and saliva immunoglobulin A (IgA), while Universitas Gajah Mada's Clinical Pathology Lab tested for serum FOXP3. All samples were collected in the morning, between 8 and 10 AM, to ensure consistency across participants.

Biochemical analysis was conducted on the collected samples. Saliva cortisol levels were measured using a commercially available Human Cortisol ELISA kit (ElabScience, Wuhan, China) and the levels were presented in ng/mL. Serum  $\beta$ -endorphin levels were assessed using the Human-EP ( $\beta$ -endorphin) ELISA kit (ElabScience, Wuhan, China), measured in pg/mL. Salivary IgA level was measured using the Human IgA ELISA kit (ElabScience, Wuhan, China), based on the saliva samples, measured in mg/mL. Serum FOXP3 level was measured using the Human FOXP3 ELISA kit (ElabScience, Wuhan, China).

The demographic characteristics of the participants in both groups were collected. This included the age, sex, length of work experience, type of occupation, educational attainment, and

ethnicity. In addition, the participants within the intervention group were also asked whether they liked or disliked the music played during the music therapy session. The possible responses were 'Do not like', 'Quite like', 'Like' and 'Very like'.

### Statistical analysis

Categorical data are presented in percentages, while numerical data are presented in averages with standard deviations or as medians and interquartile ranges. The Kolmogorov-Smirnov method was used to assess data distribution. The basic characteristics of the participants between intervention and control groups were compared using Chi-squared test or Fisher's exact test and Mann-Whitney test as appropriate. To compare the outcomes between groups, the independent Student t-test and Mann-Whitney test were used as appropriate. To compare the outcomes (immunological and neuroendocrine markers) based on the music preference during the therapy, the Mann-Whitney test and independent Student t-test were used. A  $p$ -value of  $<0.05$  was considered significant. All analytical tests were performed using SPSS version 21.0 (IBM, New York, USA).

## Results

### Participant screening and recruitment

Among the 1580 healthcare workers (physicians and nurses) who were working in Dr. Kariadi General Hospital, 814 respondents were willing to participate in the study. Initial screening (using MBI-HSS and other clinical inclusion criteria) excluded 480 participants mainly because they did not meet the inclusion criteria (463 respondents) and other reasons (17 participants) and reduced the sample to 334 participants (**Figure 1**). We randomly chose 100 participants and tested using the Mini ICD-10 questionnaire and further reduced the sample to 82 participants. Randomization using simple random sampling was conducted on 82 samples, with 41 patients receiving music therapy (intervention group) and 41 patients receiving psychoeducation (control group). During the study, one subject could not continue the study according to the dropout criteria: one patient from the intervention group and one from the control group (**Figure 1**). Detailed CONSORT flow of the study participant selection is presented in **Figure 1**.

### Characteristics of the participants

The most frequent participants included in this study were females (66.3%), aged 21–30 years (51.3%), nurses (72.5%), last education bachelors (63.7%), Javanese (91.3%) with a median work experience of 5 years (**Table 1**). Our data indicated that there was no significant difference between distributions of age, sex, length of work experience, type of occupation, educational attainment and ethnicity of the healthcare workers between groups (**Table 1**). Baseline MBI-HSS scores, collected prior to intervention, were not significantly different between the two groups ( $p=0.919$ ) (**Table 1**).

### Effects of traditional music therapy on the psychosomatic aspect of burnout syndrome

Our data indicated that the baseline MBI-HSS scores were not significantly different between the two groups. After two and four weeks of intervention, there was a significant difference between the intervention and control groups, in which the mean MBI-HSS score of the intervention group was lower than the control group ( $p=0.001$  and  $p=0.0014$ , respectively) (**Table 2**). Our data indicated that the reduction of the MBI-HSS score between week 4 and week 0 was significantly higher in the intervention group compared to the control group ( $p=0.022$ ) (**Table 2**).

### Effects of traditional music therapy on neurological aspect of burnout syndrome

The baseline HRV values were not significantly different between the two groups. After two weeks of intervention, however, HRV values of the intervention group were significantly higher than the control group ( $p=0.001$ ) (**Table 3**). There was also a significant difference between HRV in the intervention group and control group by the end of week 4 ( $p<0.0001$ ) (**Table 3**). The

improvement of the HRV between week 4 and week 0 was significantly higher in the intervention group compared to the control group ( $p<0.0001$ ) (**Table 3**).

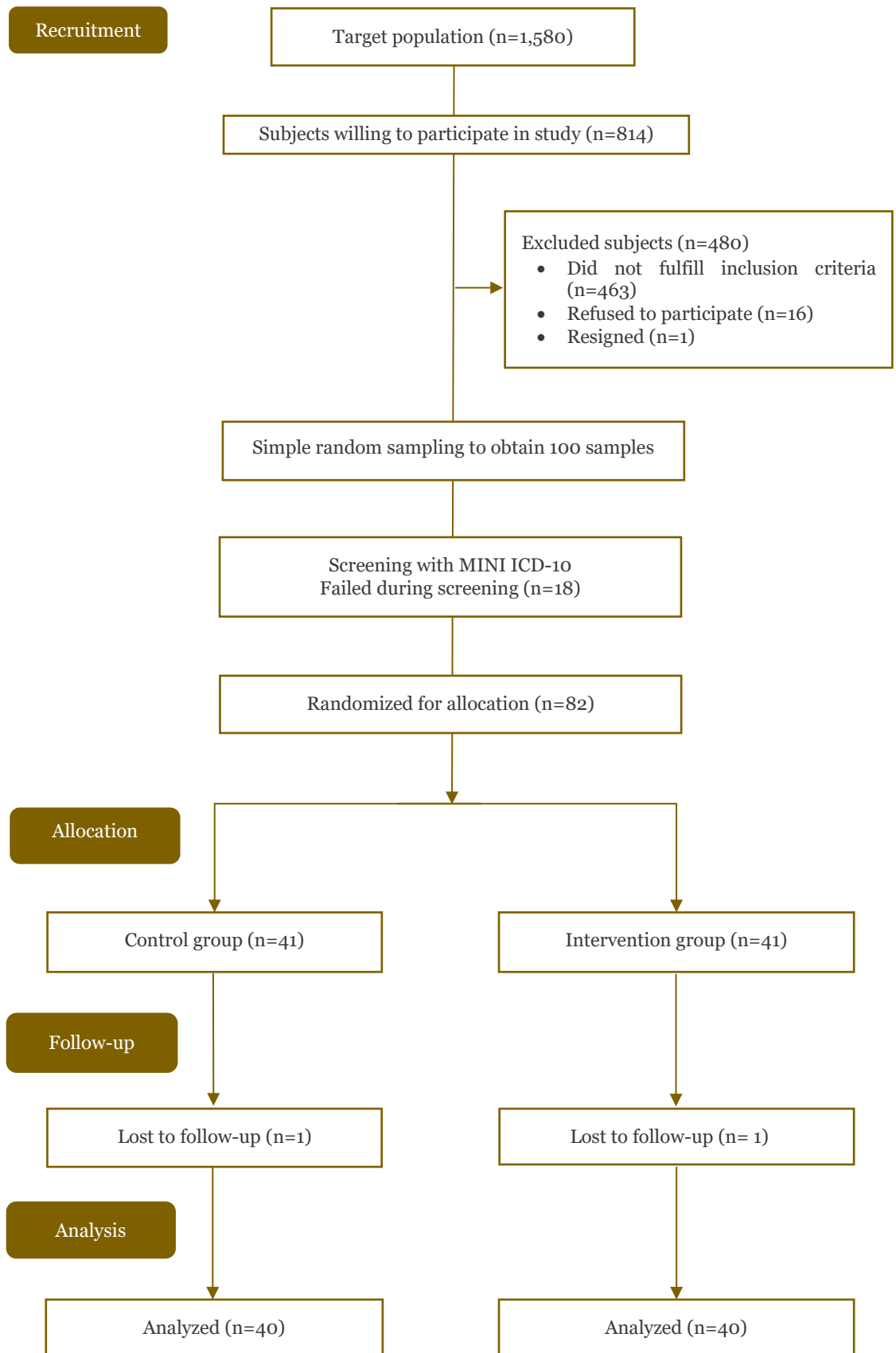


Figure 1. CONSORT flow of the study.



Table 1. Characteristics of healthcare workers included in intervention and control groups in the study (n=80)

Characteristics	Frequency (%)			p-value
	Total (n=80)	Intervention (n=40)	Control (n=40)	
Age (years)				0.251 <sup>a</sup>
21–30	41 (51.3)	17 (42.5)	24 (60.0)	
31–40	28 (35.0)	16 (40.0)	12 (30.0)	
41–50	8 (10.0)	6 (15.0)	2 (5.0)	
51–60	3 (3.7)	1 (2.5)	2 (5.0)	
Sex				0.098 <sup>b</sup>
Male	27 (33.7)	17 (42.5)	10 (25.0)	
Female	53 (66.3)	23 (57.5)	30 (75.0)	
Working experience (years), median (interquartile range)	5 (2–10)	5 (2–10)	5 (2–8)	0.892 <sup>c</sup>
Type of occupation				0.803 <sup>c</sup>
Physician	22 (27.5)	12 (30.0)	10 (25.0)	
Nurse	58 (72.5)	28 (70.0)	30 (75.0)	
Education				0.055 <sup>a</sup>
Diploma	26 (32.5)	7 (17.5)	19 (47.5)	
Bachelors	51 (63.7)	31 (77.5)	20 (50.0)	
Masters	3 (3.8)	2 (5.0)	1 (2.5)	
Ethnicity				0.119 <sup>a</sup>
Banten	1 (1.2)	1 (2.5)	0 (0.0)	
Batak	1 (1.2)	1 (2.5)	0 (0.0)	
Javanese	73 (91.3)	34 (85.0)	39 (97.5)	
Sasak	1 (1.2)	0 (0.0)	1 (2.5)	
Chinese-Indonesian	4 (5.0)	4 (10.0)	0 (0.0)	
MBI-HSS score, median (IQR)		52 (48–63)	52 (49–58)	0.919

IQR: interquartile range; MBI-HSS: Maslach Burnout Inventory-Human Services Survey

<sup>a</sup>Analyzed using Fisher's exact test<sup>b</sup>Analyzed using Chi-squared test<sup>c</sup>Analyzed using Mann-Whitney test

Table 2. Effects of traditional music therapy on psychosomatic outcome based on Maslach Burnout Inventory-Human Services Survey (MBI-HSS) between intervention and control groups

MBI-HSS	Group		p-value
	Intervention (n=40)	Control (n=40)	
Week 0, median (IQR)	52 (48–63)	52 (49–58)	0.919 <sup>a</sup>
Week 2, mean±SD	43.2±20.01	62.08±28.06	0.001 <sup>b</sup>
Week 4, mean±SD	42.2±24.51	57.38±29.06	0.014 <sup>b</sup>
Delta week 0–4, median (IQR)	-19 (-28.5–(-0.25))	-1 (-24.75–29.5)	0.022 <sup>a</sup>

IQR: interquartile range; SD: standard deviation

<sup>a</sup>Analyzed using Mann-Whitney test<sup>b</sup>Analyzed using independent Student t-test

Table 3. Effects of traditional music therapy on neurological outcome based on heart rate variability (HRV) between intervention and control groups

HRV (second)	Group		p-value
	Intervention (n=40)	Control (n=40)	
Week 0, median (IQR)	40.75 (35.68–62.38)	35.23 (29.18–54.26)	0.131 <sup>a</sup>
Week 2, median (IQR)	48.17 (35.40–60.35)	30.61 (25.93–43.36)	0.001 <sup>a</sup>
Week 4, mean±SD	54.24±17.56	39.06±13.23	<0.0001 <sup>b</sup>
Delta week 0–4, median (IQR)	53.19 (42.54–67.34)	39.62 (29.28–46.34)	<0.0001 <sup>a</sup>

IQR: interquartile range; SD: standard deviation

<sup>a</sup>Analyzed using Mann-Whitney test<sup>b</sup>Analyzed using independent Student t-test

### Effects of traditional music therapy on immunological aspect of burnout syndrome

Our data indicated that there was no significant difference in IgA levels between the two groups after two weeks ( $p=0.610$ ) and four weeks ( $p=0.851$ ) between intervention and control groups (Table 4). The data also indicated that the level changes in IgA between week 1 and week 4 were

not significantly different between intervention and control groups (0.03 mg/mL vs 0.02 mg/mL,  $p=0.821$ ) (**Table 4**).

There was no significant difference in FOXP3 levels between the intervention and control groups after two- or four-weeks of intervention with  $p=0.600$  and  $p=0.050$ , respectively. However, the level changes between pre-intervention and four-week intervention were significantly different between intervention and control groups (2.21% vs -6.17%,  $p=0.035$ ) (**Table 4**).

Table 4. Effects of traditional music therapy on immunological outcome based on immunoglobulin A (IgA) and forkhead box P3 (FOXP3) levels between intervention and control groups

Variable	Group		p-value
	Intervention (n=40)	Control (n=40)	
IgA (mg/mL)			
Week 0, median (IQR)	0.13 (0.11–0.23)	0.15 (0.10–0.24)	0.776 <sup>a</sup>
Week 2, median (IQR)	0.17 (0.11–0.29)	0.18 (0.12–0.29)	0.610 <sup>a</sup>
Week 4, median (IQR)	0.18 (0.14–0.28)	0.18 (0.14–0.29)	0.851 <sup>a</sup>
Delta week 0–4, mean±SD	0.03±0.07	0.02±0.09	0.821 <sup>a</sup>
FOXP3 (%)			
Week 0, median (IQR)	6.45 (2.52–18.72)	10.8 (2.12–23.05)	0.550 <sup>a</sup>
Week 2, median (IQR)	6.40 (2.97–10.82)	4.5 (2.35–11.70)	0.600 <sup>a</sup>
Week 4, median (IQR)	12.85 (2.12–22.4)	4.8 (1.75–10.60)	0.050 <sup>a</sup>
Delta week 0–4, mean±SD	2.21±20.59	-6.17±13.73	0.035 <sup>b</sup>

IQR: interquartile range; SD: standard deviation

<sup>a</sup>Analyzed using Mann-Whitney test

<sup>b</sup>Analyzed using independent Student t-test

### Effects of traditional music therapy on neuroendocrine aspect of burnout syndrome

Baseline  $\beta$ -endorphin and cortisol levels in week 0 were not significantly different between intervention and control groups ( $p=0.825$  and  $p=0.996$ , respectively). The two groups also had no significant differences in cortisol and  $\beta$ -endorphin levels throughout the study (**Table 5**). Although there was a trend of decreasing cortisol values in the intervention group, there was no significant difference in level changes between pre-intervention and four-week intervention between the intervention and control groups (**Table 5**).

Table 5. Effects of traditional music therapy on neuroendocrine outcomes based on  $\beta$ -endorphin and cortisol between intervention and control groups

Variable	Group		p-value
	Intervention (n=40)	Control (n=40)	
$\beta$ -endorphin (pg/mL)			
Week 0, median (IQR)	168.0 (123.0–314.0)	196.5 (118.7–339.7)	0.825 <sup>a</sup>
Week 2, median (IQR)	184.5 (115.0–232.0)	147.0 (77.5–252.2)	0.164 <sup>a</sup>
Week 4, median (IQR)	181.0 (131.0–331.0)	145.0 (110.2–310.7)	0.191 <sup>a</sup>
Delta week 0–4, median (IQR)	5 (-37.5–85.2)	-23.0 (-112.0–26.2)	0.071 <sup>a</sup>
Cortisol (ng/mL)			
Week 0, median (IQR)	7.2 (5.8–10.7)	7.7 (5.5–10.1)	0.996 <sup>a</sup>
Week 2, median (IQR)	7.6 (4.5–10.5)	7.9 (5.6–9.6)	0.634 <sup>a</sup>
Week 4, median (IQR)	6.9 (5.3–8.7)	7.9 (5.3–9.6)	0.405 <sup>a</sup>
Delta week 0–4, median (IQR)	-0.8 (-4.67–1.55)	0.0 (-3.52–3.25)	0.479 <sup>a</sup>

IQR: interquartile range; SD: standard deviation

<sup>a</sup>Analyzed using Mann-Whitney test

<sup>b</sup>Analyzed using independent t-test

### Subgroup analysis based on music preference

We next compared the laboratory results (immunological and neuroendocrine markers) of participants within the intervention group based on their thoughts about the music played during the therapy and the results are presented in **Table 6**. There was no significant difference found in IgA, FOXP3 and cortisol levels throughout intervention (all had  $p>0.05$ ). There was a significant difference in  $\beta$ -endorphin levels between groups in week 2 of intervention ( $p=0.042$ ), but this became not significant after four weeks of intervention (**Table 6**).

Table 6. Comparisons of laboratory results based on music preference among participants within intervention group (n=40)

Variable	Music preference (Likert scale)				p-value
	Do not like (n=2)	Quite like (n=4)	Like (n=15)	Very like (n=19)	
IgA (mg/ml)					
Week 0, median (IQR)	1.05 (0.09–0.12)	0.16 (0.13–0.28)	0.12 (0.09–0.31)	0.15 (0.12–0.22)	0.446 <sup>a</sup>
Week 2, median (IQR)	0.13 (0.09–0.18)	0.17 (0.11–0.27)	0.20 (0.14–0.30)	0.16 (0.10–0.26)	0.333 <sup>a</sup>
Week 4, median (IQR)	0.18 (0.12–0.24)	0.26 (0.17–0.39)	0.24 (0.15–0.32)	0.15 (0.14–0.20)	0.221 <sup>a</sup>
Delta week 0–4, median (IQR)	0.07 (0.03–0.12)	0.08 (0.04–0.11)	0.05 (–0.01–0.08)	0.01 (–0.02–0.03)	0.099 <sup>b</sup>
FOXP3					
Week 0, median (IQR)	21.5 (4.1–33.3)	11.4 (4.1–16.5)	4.9 (2.0–24.1)	5.8 (2.8–17.3)	0.792 <sup>a</sup>
Week 2, median (IQR)	7.1 (4.2–10.0)	12.9 (3.8–27.3)	6.2 (2.6–7.1)	7.1 (2.6–11.1)	0.769 <sup>a</sup>
Week 4, median (IQR)	14.6 (12.5–16.7)	6.2 (0–14.6)	13.3 (2.1–28.0)	8.6 (2.7–22)	0.591 <sup>a</sup>
Delta week 0–4, median (IQR)	–6.9 (–16.6–2.7)	–5.2 (–12.1–6.1)	0.2 (–13.4–23.9)	1.7 (–5.8–12.4)	0.758 <sup>b</sup>
β-endorphin (pg/mL)					
Week 0, median (IQR)	123 (85–161)	387 (168–597)	185 (163–299)	150 (116–209)	0.202 <sup>a</sup>
Week 2, median (IQR)	80 (58–103)	334 (203–609)	193 (166–227)	148 (112–201)	0.042 <sup>a*</sup>
Week 4, median (IQR)	113 (73–154)	347 (198–725)	205 (154–411)	175 (112–207)	0.077 <sup>a</sup>
Week 6, median (IQR)	86 (69–104)	218 (138–535)	172 (129–245)	157 (103–188)	0.321 <sup>a</sup>
Delta week 0–4, median (IQR)	–9.5 (–12–(–7))	30 (–40–197)	64 (–16–106)	–10 (–50–46)	0.473 <sup>a</sup>
Cortisol (ng/mL)					
Week 0, median (IQR)	9.7 (9.2–10.3)	6.9 (2.6–10.5)	7.2 (6.1–11.3)	6.7 (5.8–9.7)	0.675 <sup>a</sup>
Week 2, median (IQR)	6.3 (5.1–7.5)	9.0 (3.6–15.0)	7.7 (4.6–10.1)	8 (4.5–9.6)	0.944 <sup>a</sup>
Week 4, median (IQR)	8.5 (5.8–11.2)	9.1 (6.7–11.9)	6.4 (5.9–7.7)	6.9 (4.8–8.9)	0.478 <sup>a</sup>
Delta week 0–4, median (IQR)	–1.2 (–3.4–0.9)	2.9 (–2.0–7.5)	–0.8 (–4.3–0.4)	–1 (–5.3–1.2)	0.581 <sup>a</sup>

IQR: interquartile range

<sup>a</sup>Analyzed using Mann-Whitney test<sup>b</sup>Analyzed using independent Student t-test\*Statistically significant at  $p < 0.05$



## Discussion

This study was conducted to investigate the effects of traditional music therapy on psychological, neurological, immunological, and endocrine responses in healthcare workers. The demographic characteristics of the study samples were comparable to those reported in previous studies [23-25]. Our findings indicated that traditional music therapy improved psychological outcomes (MBI-HSS score), neurological function (HRV), immunological markers (IgA, FOXP3), and endocrine responses ( $\beta$ -endorphin and cortisol) in healthcare workers experiencing BOS.

Significant differences were observed in the MBI-HSS results after two and four weeks of music therapy, highlighting its positive effect on BOS. This finding aligns with a previous study that reported a decreased risk of BOS among healthcare workers following music therapy [26]. In the present study, a significant difference in post-test HRV values between the intervention and control groups further demonstrated the positive impact of music therapy. Higher HRV serves as a biomarker of an individual's capacity to respond to stress [27]. Autonomic dysregulation in BOS is primarily driven by increased sympathetic nervous system activity or elevated cortisol levels in response to acute stress [28].

Both FOXP3 and IgA hold promise as potential biomarkers for assessing chronic stress. IgA plays a crucial role as an anti-inflammatory agent in the body, although the mechanisms underlying the effect of music on IgA levels are not yet fully understood [29,30]. The insignificant findings in this study may be attributed to the immunosuppressive effects of chronic stress, mediated by elevated cortisol levels. A previous study has shown that a decrease in CD19+ B cell levels is inversely proportional to cortisol levels [29]. FOXP3 also suppresses inflammation through various mechanisms, including reducing the activation of effector T cells and promoting the production of anti-inflammatory cytokines such as IL-10. In humans, regulatory T cell levels are reduced in individuals with mood disorders and major depressive disorders [31-33]. Although both FOXP3 and IgA have potential as biomarkers, further research is required to better understand the factors influencing changes and dysregulation of these biomarkers.

Throughout the study, cortisol levels in both groups showed no significant differences. However, there was a trend of decreasing cortisol levels in the intervention group and an opposite trend in the control group, although the changes were negligible. This finding aligns with previous studies that demonstrated a strong association between listening to music and reduced cortisol levels [34,35]. Despite these findings, a systematic review identified other potential biomarkers of chronic stress, including adrenocorticotrophic hormone, brain-derived neurotrophic factor, C-reactive protein, prolactin, oxytocin, and dehydroepiandrosterone [36]. Consequently, cortisol may not be the most suitable biomarker for assessing the endocrine effects of music therapy on BOS.

Our data also indicated no significant difference in  $\beta$ -endorphin levels between the two groups. However, a trend of increasing  $\beta$ -endorphin levels in the intervention group and a decrease in the control group was observed. Given the role of  $\beta$ -endorphin in producing feelings of euphoria and well-being, it is intuitive to expect low  $\beta$ -endorphin levels in depression. Nevertheless, a study by Alonso *et al.* reported that plasma  $\beta$ -endorphin levels were significantly elevated in patients with major depression [37]. Interestingly, our study found a significant difference in  $\beta$ -endorphin levels between participants who liked the music provided and those who did not. Different cultures have unique musical traditions, genres, and rhythms deeply rooted in their communities [38]. Music perceived as pleasant enhances the intensity of emotional valence, thereby reducing stress [39]. Therefore, music preferences and sociocultural backgrounds are essential considerations when providing traditional music therapy.

In the present study, music therapy was administered for four weeks, with a frequency of 3–4 sessions per week and a duration of 45 minutes per session. Variations in these parameters may influence the therapeutic outcomes. According to a meta-analysis, the most effective regimen involved 4–6 weeks of therapy, with a frequency of less than three sessions per week and session durations exceeding 60 minutes [40]. However, these differences were not statistically significant compared to other variations in the duration, frequency, and period of the same music therapy [40]. Based on the literature, the music therapy regimen used in this study appears to be optimal. Nonetheless, further research is warranted to explore the impact of different durations, frequencies, and therapy periods to enhance BOS outcomes.

To our knowledge, this was the first study to utilize traditional Indonesian music as a therapy for BOS among health workers and the first to use laboratory biomarkers to evaluate its therapeutic effects and effectiveness. However, this study has several limitations. The intervention period was relatively short, with a minimal therapeutic dose, and such short-term interventions may not significantly influence various endocrine and immunological aspects in patients with BOS. Furthermore, the research was conducted in real-world settings, making it challenging to control external stressors such as increased workloads and non-work-related issues. The study highlights several areas for improvement in future research. Extending the intervention period could help better assess long-term effects, while increasing the frequency and duration of therapy sessions might capture more significant changes in biological markers. Additionally, combining music therapy with other non-pharmacological approaches, such as psychotherapy, could offer deeper insights into potential synergistic or antagonistic effects. Future studies are also encouraged to investigate the use of traditional music therapy across diverse cultural contexts to ensure its broader applicability and effectiveness.

## Conclusion

This study demonstrated that traditional music therapy positively influenced the psychological, neurological, immunological, and endocrine aspects of BOS in healthcare workers. These effects were respectively represented by improvements in the MBI-HSS score, HRV, IgA, FOXP3,  $\beta$ -endorphin, and cortisol levels. Traditional music therapy is recommended as a non-pharmacological intervention, contributing to a holistic approach to managing BOS.

## Ethics approval

This study is based on the Declaration of Helsinki and Guidelines for Good Clinical Practice from the international conference on harmonization tripartite guidelines (ICH-GCP) and the regulations in Indonesia. This study has been approved by the local Ethical Committee (S-22288/UN2/F1.D/PDP.01/2023 and DP.04.01/D.X.2/12009/2023), and all participants signed an informed consent form before enrollment.

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## Competing interests

All the authors declare that there are no conflicts of interest.

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## Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

## Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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