Using Music as a Tool for Distress Reduction During Cancer Chemotherapy Treatment

Felicity W.K. Harper, PhD[1,2]; Allison S. Heath, BS[1]; Tanina Foster Moore, PhD[1,2]; Seongho Kim, PhD[1,2]; and Elisabeth I. Heath, MD[1,3]

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ABSTRACT

PURPOSE Music may be an effective therapeutic tool during cancer treatment to improve patient psychological and physical well-being. Current research shows a positive effect of music on psychological outcomes; however, many of these studies lacked significant sample size and rigor in monitoring type of music used and duration of music use during treatment.

METHODS Participants (N = 750) in this open-label, multisite, day-based permuted block randomization study were adult patients receiving outpatient chemotherapy infusion. Patients were randomly assigned to either music (listen to music for up to 60 minutes) or control (no music) conditions. Music patients were allowed to self-select an iPod shuffle programmed with up to 500 minutes of music from a single genre (eg, Motown, 60s, 70s, 80s, classical, and country). Outcomes were self-reported change in pain, positive and negative mood, and distress.

RESULTS Patients who listened to self-selected music during infusion showed significant benefit in improved positive mood and reduced negative mood and distress (but not pain) from pre- to post-intervention (all two-sample t-tests $P < .05$). LASSO penalized linear regression models showed a selective benefit for some patients on the basis of relationship ($P = .032$) and employment ($P = .029$) status with those who were married or widowed and those on disability showing better outcomes.

CONCLUSION Music medicine is a low-touch, low-risk, and cost-effective way to manage patients' psychological well-being in the often stressful context of a cancer infusion clinic. Future research should be directed to understanding what other factors may mitigate negative mood states and pain for certain groups during treatment.

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INTRODUCTION

Nearly 1.5 million new cancer cases are diagnosed each year.[1] Many of these patients will undergo chemotherapy as part of their treatment. Common side effects include pain, fatigue, nausea, vomiting, anxiety, depression, and hair loss,[2] which can not only take a toll physically but also be emotionally overwhelming and stressful.[3]

Music medicine is the use of music to reduce negative emotional states and aid in stress management and emotional expression. Whether listening passively or actively, music has been found to be an effective nonpharmacologic intervention for patients undergoing cancer treatment.[4,5] Both physical (ie, pain and fatigue) and psychological outcomes (ie, distress and mood) have been positively affected by music during treatment.[4-12] Previous studies have also shown that adult patients with cancer are interested in music interventions.[10]

However, meta-analyses in this area have shown limitations to previous studies, including small sample size and weak methodology, such as lack of detailed description of selected music and lack of consideration of potential confounders (eg, patients' musical background).[4,11,13] To better understand the clinical benefit of music as an adjunct treatment during chemotherapy, additional studies must be done with larger sample sizes and more rigorous methodology.

The current study used an open-label, multisite, day-based permuted block randomization design to test music as a therapeutic intervention to improve pain, mood, and distress in patients during chemotherapy infusion. A key feature of this study was accounting for limitations in the existing literature. Specifically, the study recruited a large cohort, providing significantly more power than many previous studies.[13] In addition, the study assessed participants'

CONTEXT

Key Objective

This study used a large sample and a methodologically rigorous open-label, multisite, day-based permuted block randomization design to test the benefits of music as a low-risk and low-cost intervention to improve pain, mood, and distress in patients during chemotherapy infusion.

Knowledge Generated

There were significant differences in change in positive and negative mood and distress (although not pain) from pre- to post-intervention between the music and control groups. Participants who were married or widowed and those receiving disability income reported greater benefit outcomes after listening to music.

Relevance

Music medicine is a low-touch, low-risk, and cost-effective way to manage patients' psychological well-being during chemotherapy infusion.

musical preference, the impact of previous training in voice or music, sociodemographics, and clinical features as correlates.

Primary Aim

1. To test the effect of listening to music on patients' pain, mood, and level of distress during chemotherapy infusion.

Hypothesis

Patients with cancer who listen to music will have a greater reduction in negative mood, pain, and distress from pre- to post-intervention and more improvement in positive mood than those who do not listen to music.

Secondary Aim

1. To explore correlates (ie, previous training in voice or music, and patients' sociodemographics, clinical features, and self-reported anxiety and depression) of change in outcomes from pre- to post-intervention.

METHODS

Participants

The sample was 750 patients receiving chemotherapy infusion from February 2018 to March 2020 at Karmanos Cancer Institute (Detroit, MI) and five affiliated McLaren Health clinics throughout the state of Michigan (a total of six sites). Eligibility criteria were (1) age >18 years, (2) able to speak, read, write, and understand English, (3) sufficient hearing capacity to hear music, and (4) scheduled for a chemotherapy infusion lasting ≥60 minutes. Patients with cognitive or perceptual disturbances were excluded (caregivers were also recruited using the same eligibility criteria; however, this study focuses specifically on the patients in this study). Institutional review boards at Wayne State University and Karmanos Cancer Institute provided approval for all study procedures.

Procedure

Members of the clinical care team in each infusion clinic identified participants who met eligibility criteria. Interested patients were referred to a member of the research team who explained the study procedures, provided the participant with an opportunity to ask questions, and obtained written informed consent. The research assistant also described the amount of time that the participant would be involved in the study and ensured that they understood that participation was voluntary and would have no impact on current or future medical care. After providing consent, participants completed a brief questionnaire assessing (1) sociodemographic characteristics (ie, age, sex, race/ethnicity, and household income), (2) musical background (eg, training in voice or a musical instrument), (3) anxiety and depression, and (4) baseline levels of pain, mood, and distress. The explanation of the study, consent, and questionnaire took approximately 15-20 minutes to complete.

At the time of consent, participants were assigned to the control or intervention group depending on the day of the week. Days within a week were block-randomized such that any given day, music was provided to participants (*intervention day*) or no music was provided to participants (*control day*).

Music participants were asked to select a musical genre for the 60-minute listening period. Examples included Motown, 60s, 70s, 80s, classical, and country. Each participant was provided with an iPod shuffle, programmed with approximately 150 songs (up to 500 minutes) of music from that genre. The iPods were distributed by research nurses or individuals who had completed hospital volunteer training.

To ensure the safe use of iPods across multiple participants, the handling and disinfection of iPods followed Karmanos Cancer Institute policies on antiseptics, disinfectants, and infection control, and all participants received a new pair of one-time-use headphones. After the listening period, music participants completed a postsurvey assessing pain, positive and negative mood, and distress levels. They also recorded the amount of time spent listening to music.

The control group served as an active waitlist control for participants who were recruited on days designated as nonmusic days. The control group completed pre- and post-surveys across a 60-minute period to mirror the timing of surveys for the intervention group but was instructed not to listen to music during the study period. Given the potentially beneficial effect of music, control participants were given the option to listen to music using one of the study iPods after they had completed their participation. Participants in both groups received $10 in US dollars (USD) gift cards for their participation.

Measurable Variables

The primary end points were change in self-reported pain, positive and negative mood, and distress from pre- to post-intervention. A visual analog scale was used for participants to rate their pain from 0 (*no pain*) to 10 (*worst imaginable pain*).[5] The Positive and Negative Affect Scale (PANAS) was used to assess participant's mood. This measure is widely used to assess state-dependent levels of positive and negative mood.[14] The Distress Thermometer was used to assess participant distress from 0 (*no distress*) to 10 (*extreme distress*). This measure is part of the National Comprehensive Cancer Network Practice Guidelines and is commonly used to measure distress.[8]

Other measured variables were study site (a total of six sites), sociodemographics (ie, age, sex, race, education level, relationship status, employment status, and household income), musical preference, musical training (ie, voice and musical instrument), and clinical variables (ie, cancer stage and type of treatment). Participants also completed the Hospital Anxiety and Depression Scale, a well-validated measure of anxiety and depressive symptoms in patient populations, to control for any baseline effect of pre-existing mood.[25] Participants were also asked if they have taken any antianxiolytic or allergy medication (eg, Xanax, Benadryl) before their infusion to also control for any effects on baseline mood.

Design

The study used a randomized two-arm pre-post design. As the intervention could not be feasibly blinded to the control arm, day-based permuted block randomization was used. All participants who enrolled in the study on an intervention day (ie, music day) were assigned to the intervention arm, while those who enrolled on a control day (ie, nonmusic day) were assigned to the control arm. At the Karmanos infusion center, most of patients receive week-based chemotherapy on either Tuesday or Thursday. Therefore, two day-based randomized block designs were used. The first block (Monday, Wednesday, and Friday) was randomized across 2 weeks with a weighted block size of 3 (first week: 2 intervention days and 1 control day, and second week: 1 intervention day and 2 control days). The second block (Tuesday and Thursday) was randomized every week with block size of 2. As all six sites were expected to have a similar distribution of patients per day, the same day-based randomized block design was used across sites.

The accrual target was set at 750 participants (ie, 375 per group). Assuming an attrition rate of 10%, the power for primary outcomes was justified with 674 participants (ie, 337 per group) using an unpaired t-test. This number assumed a small effect size ($d = 0.2$) with >95% power to detect a true difference between two groups when a two-sided unpaired t-test was used at a $P \leq 5\%$ significance level. Even applying a Bonferroni multiple comparison correction for up to 10 variables, a sample size of 674 participants had >80% power to detect a true difference using a two-sided 0.5% (5%/10) level.

Data Analysis

Baseline characteristics were summarized using count and percentage for categorical variables, and mean and standard deviation (SD) for continuous variables. Continuous outcomes were checked for distributional assumptions. Change in the four outcomes (pain, mood [PANAS positive and PANAS negative], and distress) was calculated as the difference from pre- to post-intervention. Comparisons between groups (music *v* control) were performed using two-sample unpaired t-tests corrected for multiplicity with the Holm's procedure. Cohen's d with 95% confidence intervals (CI) were used as a measure of clinical significance. A multivariable linear regression analysis was carried out with 11 baseline characteristics (intervention group, sex, race [*White v non-White*], education level, relationship status, employment status, household income, cancer treatment, cancer stage, anxiety/allergic medication, training in musical instrument(s), or voice training [*yes v no*]) as predictors of change of each of the four outcomes. LASSO-based penalized linear regression models with leave-one-out cross-validation were used to avoid underpowered analyses. Multivariable linear regression analyses for each outcome were then performed with the LASSO-selected baseline characteristics. P values were further corrected using the Holm's procedure to account for multiple comparisons.

RESULTS

Sample

The average participant (N = 708; Fig 1) was 60.39 years old and female (65%). Twenty-eight percent of the sample

identified as African American; the remainder were White (68%) or other ethnicities (1% Asian, 1% American Indian/Native Alaskan, and 2% multiracial). The majority were married or in a committed relationship (56%) and had a household income <$40,000 (USD) per year (40%). An additional 20% reported income <$60,000 (USD) per year. Only 25% reported full-time employment with the majority being retired (35%) or disabled (24%). Forty-one percent had a high school education or less with an additional 24% having some college. The majority of participants had advanced (stage III or IV) cancer (58%), and 30% indicated they took anxiety/allergy medication before their appointment (Table 1).

The most frequently selected music genre was *Motown* (28%) followed by *hits from the 80s* (20%). The majority of intervention participants (90%) indicated they were *very satisfied* or *quite satisfied* with their music selection and listened to music for an average of 56.68 (SD = 8.23) minutes out of a possible 60-minute listening period. White patients had an even distribution of musical selection across all genres; by contrast, 65.4% of African American patients selected Motown for their musical genre.

Intervention Effects

There were no preintervention differences in pain, positive or negative mood, or distress levels between the music and control groups (all P_{adj} values approaching 1.0). By contrast, there were significant differences (or trends $P < .10$) for all outcome measures at post-test ($P_{adj} = .004$-$.072$). Music participants reported more positive and less negative mood, less distress, and lower pain postprocedure than control participants.

Change in Outcomes

As shown in Table 2, there was significant difference in change for three of the four outcomes (positive and negative mood and distress) between the music and control groups. However, there was no significant difference in change for pain between groups. There were also no differences in change outcomes on the basis of having a companion participate in the intervention (all $P > .05$).

Multivariable Analysis

A two-step process was used to explore covariates of change from pre- to post-intervention. First, LASSO penalized linear regression models with leave-one-out cross-validation were used to identify subsets of significant predictors among the set of 11 possible covariates for each outcome. No covariates were selected for change in negative mood; therefore, this outcome was dropped from further analysis. In a second step, multivariable models were constructed using the LASSO-selected subset of covariates for the three remaining outcomes (positive mood, pain, and distress). As shown in Table 3, positive mood was significantly associated with both intervention group assignment ($P_{adj} = .002$) and relationship status (global $P_{adj} = .032$). Specifically, participants in the music group had higher positive mood compared with those in the control group, and participants who were married or widowed were more likely to experience an improvement in mood than divorced, separated, or never married patients. Change in distress was not related to relationship status but was related to employment status (global $P_{adj} = .029$). Participants receiving disability income reported greater reductions in distress postintervention ($\beta = -.453$ [.227]; $P_{adj} = .047$) compared with those who were employed full-time or retired.

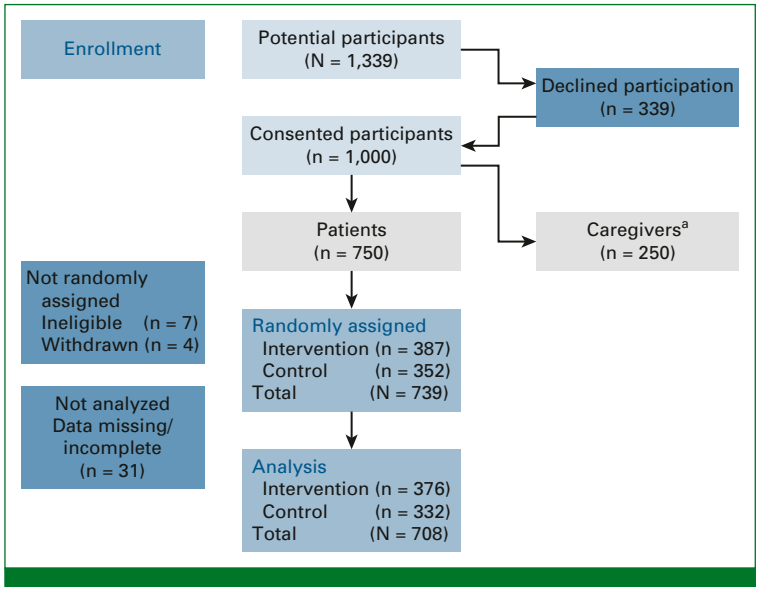

FIG 1. CONSORT diagram. [a]Not analyzed in this study.

TABLE 1. Patient Baseline Characteristics

Participants	Control (n = 332)	Music (n = 376)	All (N = 708)
Age, years, mean (SD)	60.54 (12.59)	60.26 (12.43)	60.39 (12.50)
Missing	*4*	*12*	*16*
Sex, No. (%)			
Male	112 (34)	135 (36)	247 (35)
Female	220 (66)	240 (64)	460 (65)
Missing	*0 (0)*	*1 (0)*	*1 (0)*
Hispanic or Latino/Latina, No. (%)			
Yes	6 (2)	9 (2)	15 (2)
No	325 (98)	363 (97)	688 (97)
Missing	*1 (0)*	*4 (1)*	*5 (1)*
Arab or Chaldean, No. (%)			
Yes	1 (0)	8 (2)	9 (1)
No	329 (99)	365 (97)	694 (98)
Missing	*2 (1)*	*3 (1)*	*5 (1)*
Ethnic, No. (%)			
African American or Black	93 (28)	107 (29)	200 (28)
White	225 (68)	255 (68)	480 (68)
Asian	3 (1)	1 (0)	4 (1)
American Indian or Native Alaskan	4 (1)	2 (1)	6 (1)
Middle Eastern	1 (0)	2 (1)	3 (0)
Other race or multiple races (please specify)	6 (2)	8 (2)	14 (2)
Missing	*0 (0)*	*1 (1)*	*1 (0)*
Education level, No. (%)			
Less than high school	16 (5)	24 (6)	40 (6)
High school/GED	121 (36)	123 (33)	244 (35)
Some college	76 (23)	97 (26)	173 (24)
Two-year college degree	38 (11)	38 (10)	76 (11)
Four-year college degree	54 (16)	59 (16)	113 (16)
Graduate/professional degree	27 (8)	32 (9)	59 (8)
Missing	*0 (0)*	*3 (1)*	*3 (0)*
Relationship status, No. (%)			
Married	172 (52)	168 (45)	341 (48)
Living with a partner in a marriage-like relationship	18 (5)	35 (9)	53 (8)
Widowed	31 (9)	29 (8)	60 (9)
Divorced	41 (12)	69 (18)	110 (16)
Separated	12 (4)	13 (4)	25 (4)
Never married	56 (17)	60 (16)	116 (16)
Missing	*1 (0)*	*2 (1)*	*3 (0)*
Employment status, No. (%)			
Employed full-time	85 (26)	93 (25)	178 (25)
Employed part-time	22 (7)	21 (6)	43 (6)
Homemaker	13 (4)	14 (4)	27 (4)
Unemployed	14 (4)	22 (6)	36 (5)
Retired	118 (36)	132 (35)	250 (35)
Disability	80 (24)	87 (23)	167 (24)
Missing	*0 (0)*	*7 (2)*	*7 (1)*
Household income, No. (%)			
Less than 20,000	67 (20)	82 (22)	149 (21)
20,000-39,999	62 (19)	71 (19)	133 (19)

(continued on following page)

TABLE 1. Patient Baseline Characteristics (continued)

Participants	Control (n = 332)	Music (n = 376)	All (N = 708)
40,000-59,999	71 (21)	70 (19)	141 (20)
60,000-79,000	47 (14)	58 (15)	105 (15)
≥80,000	58 (18)	53 (14)	111 (16)
Missing	*27 (8)*	*42 (11)*	*69 (10)*
Cancer stage, No. (%)			
Stage 0	6 (2)	6 (2)	12 (2)
Stage I	32 (10)	29 (8)	61 (9)
Stage II	33 (10)	58 (15)	91 (13)
Stage III	86 (26)	102 (27)	188 (27)
Stage IV	116 (35)	104 (28)	220 (31)
Missing	*59 (18)*	*77 (21)*	*136 (19)*
Cancer treatment, No. (%)			
Chemotherapy only	274 (83)	313 (83)	587 (83)
Other treatment or multiple treatments	58 (18)	60 (16)	118 (17)
Missing	*0 (0)*	*3 (1)*	*3 (0)*
Anxiety/allergic medication, No. (%)			
No	228 (69)	257 (68)	485 (69)
Yes	102 (31)	113 (30)	215 (30)
Missing	*2 (1)*	*6 (2)*	*8 (1)*
Musical training, No. (%)			
Musical instrument			
No	196 (59)	202 (54)	398 (56)
Yes	133 (40)	171 (46)	304 (43)
Missing	*3 (1)*	*3 (1)*	*6 (1)*
Training to sing			
No	284 (86)	312 (83)	596 (84)
Yes	45 (14)	61 (16)	106 (15)
Missing	*3 (1)*	*3 (1)*	*6 (1)*
Listen to music, No. (%)			
I don't usually listen to music	5 (2)	8 (2)	13 (2)
I sometimes listen to music	102 (31)	100 (27)	202 (29)
I often listen to music	140 (42)	175 (47)	315 (45)
I always listen to music	82 (25)	90 (24)	172 (24)
Missing	*3 (1)*	*3 (1)*	*6 (1)*
Site, No. (%)			
Detroit	166 (50)	170 (45)	336 (48)
Northern	66 (20)	65 (17)	131 (19)
Bay City	47 (14)	56 (15)	103 (15)
Macomb	33 (10)	63 (17)	96 (14)
Lapeer	20 (6)	22 (6)	42 (6)

NOTE. *Missing* indicates declined to answer.
Abbreviations: GED, General Educational Development test; SD, standard deviation.

DISCUSSION

Music has been used as an effective therapeutic tool for helping patients to improve, restore, or maintain health.[15,16] Music has been shown to have positive effects on physical (ie, pain and fatigue) as well as psychological (ie, mood and quality of life) outcomes during cancer treatment.[11,12,17] Given that patients receiving chemotherapy can experience high levels of distress, the ease, low cost, and safety of the intervention suggest it might have ideal application in the fast-paced but often stressful context of a cancer infusion clinic. This study proposed to address some of the methodologic limitations of previous studies on music therapy by testing the benefit of a receptive and self-guided music therapy intervention during chemotherapy infusion.

TABLE 2. Comparison Between Control and Music Group for Preoutcomes, Postoutcomes, and Pre- to Post-Intervention Change

Group	PANAS Positive	PANAS Negative	Distress	Pain
Control (n = 332), mean (SD)				
Pre	29.60 (8.53)	15.33 (6.28)	2.34 (2.40)	2.24 (2.37)
Post	29.73 (9.50)	14.45 (5.96)	1.99 (2.34)	2.00 (2.31)
Change	0.14 (5.46)	−0.88 (4.24)	−0.35 (1.58)	−0.24 (1.14)
Music (n = 376), mean (SD)				
Pre	29.82 (8.82)	14.84 (5.38)	2.22 (2.42)	2.02 (2.49)
Post	31.36 (9.80)	13.12 (4.59)	1.54 (2.19)	1.68 (2.35)
Change	1.55 (5.99)	−1.72 (3.43)	−0.67 (1.96)	−0.34 (1.32)
All (N = 708), mean (SD)				
Pre	29.71 (8.68)	15.07 (5.82)	2.28 (2.41)	2.12 (2.43)
Post	30.60 (9.69)	13.74 (5.31)	1.75 (2.27)	1.83 (2.33)
Change	0.88 (5.79)	−1.33 (3.85)	−0.52 (1.80)	−0.29 (1.24)
Preoutcomes				
P[a]	.740	.270	.481	.225
Adjusted *P*[b]	.962	.900	.962	.900
Postoutcomes				
P[a]	.026	**.001**	**.008**	.072
Adjusted *P*[b]	.052	**.004**	**.024**	.072
Change				
P[a]	**.001**	**.004**	**.016**	.316
Adjusted *P*[b]	**.004**	**.012**	**.032**	.316
Cohen's *d* (CI)[c]	**−0.245 (−0.39 to −0.097)**	**0.219 (0.071 to 0.367)**	**0.18 (0.032 to 0.328)**	0.076 (−0.073 to 0.223)

NOTE. The change of each outcome is the difference from preintervention to postintervention.
Abbreviations: PANAS, Positive and Negative Affect Scale; SD, standard deviation.
[a]Two-sided two-sample *t*-test. Bolded values indicate those that reached statistical significance. $P \le 0.05$. $P \le 0.01$. $P \le 0.001$.
[b]Corrected for multiple comparisons by the Holm's procedure.
[c]Cohen's *d* and CIs were used as indicators of clinical significance. Cohen's $d = 0.2$ is considered a small effect size. CI = 95% confidence interval. CIs not containing zero are significant.

As expected, the findings provide support for the benefit of music as an intervention during infusion. Participants who listened to music reported significantly more positive and less negative, less distress, and lower pain postintervention than those in the control group. However, there was no significant change from pre- to post-intervention for pain. It is possible that pain is not amenable to such a brief intervention, particularly because the pain that patients with cancer experience is not transient. The often ongoing and prolonged treatment-related pain experienced by patients with cancer may be driven more by physiologic sensations of pain than psychological perceptions of pain, and as such, may be less responsive to nonpharmacologic intervention.[18,19]

The second research question examined the potential effects of covariates on change in outcomes. For positive mood, there was a selective benefit of relationship status; those who are married or widowed were more likely to experience an improvement in mood than divorced and separated patients. Previous research in general shows that married people have greater subjective well-being than those who are separated or divorced, and further, those who are divorced or separated are at greater risk for poor health outcomes, including higher mortality rates.[20-24] It is possible that divorced and separated people are juggling a consistently elevated level of emotional and/or practical demands as a result of their relationship discord. For example, coparenting, changes in income and/or living situation, and even the lack of close support may lead to more chronic distress that is not easily mitigated by a music intervention. Notably, there were no significant differences by relationship status in positive mood before the intervention, underscoring the possibility that persistent distress, even at low levels, may not be responsive to state-based mood-enhancing interventions such as music medicine among certain groups.

There was also a selective benefit for distress on the basis of employment status. Patients who were on disability reported a greater reduction in distress than any other employment category (ie, employed full- or part-time, unemployed, retired, or working within the home). Perhaps participants on medical disability have greater overall stress because of the challenges of a chronic health condition(s) (eg, logistics of care, transportation, and financial aspects of care), and

TABLE 3. Multivariable Linear Regression Analyses of Factors Associated With Change From Pre- to Post-Intervention

	PANAS Positive[a]			Distress[a]			Pain[a]		
Outcome Measures	Estimate (SE)	*P*	Adjusted *P*[b]	Estimate (SE)	*P*	Adjusted *P*[b]	Estimate (SE)	*P*	Adjusted *P*[b]
Group		**.001**	**.002**		.100	.100			
Control	Reference			Reference					
Music	1.552 (0.465)			−0.250 (0.151)					
Race		.200	.200						
Caucasian	Reference								
Non-Caucasian	0.709 (0.553)								
Education level		.461[c]	.461		.205[c]	.410			
Less than high school	Reference			Reference					
High school/GED	−0.219 (1.108)	.843		−0.638 (0.350)	.069				
Some college	−0.686 (1.132)	.545		−0.624 (0.357)	.081				
Two-year college degree	0.236 (1.266)	.852		−1.017 (0.397)	**.011**				
Four-year college degree	−0.609 (1.258)	.628		−0.678 (0.390)	.083				
Graduate/professional degree	1.106 (1.398)	.429		−0.899 (0.431)	**.037**				
Relationship status		**.011[c]**	**.032**		.060[c]	.120		.847[c]	.847
Married	Reference			Reference			Reference		
Living with a partner in a marriage-like relationship	0.040 (0.909)	.965		0.232 (0.283)	.413		−0.042 (0.184)	.819	
Widowed	0.800 (0.878)	.363		−0.215 (0.297)	.471		−0.205 (0.174)	.241	
Divorced	−1.622 (0.717)	**.024**		−0.151 (0.222)	.496		−0.003 (0.137)	.981	
Separated	−3.658 (1.261)	**.004**		0.395 (0.424)	.352		−0.121 (0.258)	.638	
Never married	−0.447 (0.751)	.552		0.615 (0.232)	**.008**		0.054 (0.134)	.684	
Employment status		.071[c]	.071		**.014[c]**	**.029**			
Employed full-time	Reference			Reference					
Employed part-time	−2.446 (1.047)	**.020**		−0.202 (0.337)	.550				
Homemaker	−1.499 (1.319)	.256		0.043 (0.442)	.922				
Unemployed	0.386 (1.185)	.745		0.502 (0.369)	.174				
Retired	0.174 (0.640)	.786		0.231 (0.210)	.272				
Disability	0.656 (0.723)	.364		−0.453 (0.227)	**.047**				
Household income		.259[c]	.518						
<20,000	Reference								
20,000-39,999	0.311 (0.744)	.676							
40,000-59,999	−1.131 (0.768)	.141							
60,000-79,000	0.190 (0.938)	.840							
≥80,000	−0.514 (0.941)	.585							
Musical training (instrument or singing)		.190	.380						
No	Reference			Reference					
Yes	−0.642 (0.489)			−0.163 (0.159)	.307	.380			
Cancer stage					.211[c]	.211			
Stage 0				Reference					
Stage I				0.559 (0.588)	.343				
Stage II				0.037 (0.571)	.948				
Stage III				0.533 (0.554)	.337				
Stage IV				0.487 (0.553)	.378				

Abbreviations: GED, General Educational Development test; PANAS, Positive and Negative Affect Scale.

[a]Covariate variables selected by LASSO penalized linear regression models with leave-one-out cross-validation. No covariates were selected for the change of PANAS negative and depression.

[b]Corrected for multiple comparisons across outcomes by the Holm's procedure. Bolded values indicate those that reached statistical significance. $P \le 0.05$. $P \le 0.01$. $P \le 0.001$.

[c]Global *P* values calculated by likelihood ratio tests.

therefore, are more responsive to efforts designed to engender relaxation, reflection, and distraction.[17]

Interestingly, negative mood was not selected by the LASSO regression despite the significant changes from pre- to post-intervention. LASSO-based variable selection is based on a linear combination of covariates, and it is possible that negative mood has more complicated and/or nonlinear associations with music as an intervention. Although this exploration is beyond the scope of this research, future studies might benefit from exploring these types of models.

There were no significant effects of race, household income, cancer stage, or exposure to musical training on outcomes as has been considered in previous studies. The majority of patients were White with advanced cancer (stage III or IV) and household incomes ≤$60,000 (USD)/y, who were receiving chemotherapy as their only treatment. Perhaps the sample was sufficiently homogeneous with respect to these contextual factors such that there was not enough variability to have any meaningful effect. The majority of patients also reported listening to music with some frequency at home, so it is possible that the familiarity of listening to music, especially when combined with the ability to choose the music genre, is a uniformly pleasant experience without regard for most demographic or clinical factors.

This study has several potential limitations to note. First, the effect sizes for change in positive and negative mood and distress were small, and future research would benefit from exploration of how to enhance these outcomes. Second, the intervention was largely self-directed, and it is possible that the use of a music therapist would introduce factors such as therapeutic rapport, more time spent with the patient, and directed instructions about the benefits of music that would have yielded different results. Yet, this remains an empirical question, and the benefits of a low-cost, low-risk, and low-touch intervention cannot be overstated especially for under-resourced cancer care settings. Finally, this study did not test the benefit of music relative to other potential relaxation strategies (eg, watching television and reading) that are readily available to patients during infusion. Understanding the benefit of music in comparison with these other low-touch, cost-effective alternatives might provide additional clinical guidance about the use of these non-pharmacologic interventions during infusion.

In conclusion, the results of this rigorously designed large-scale, randomized trial of music medicine stand as evidence for the benefit of a music intervention for patients during chemotherapy infusion. Listening to music has clinical benefit for improving positive mood and reducing negative mood and distress. Other findings suggest that there may be selective benefits of music for some patients on the basis of relationship and employment status, and future research should likely be directed to understanding what other factors may mitigate negative mood states and pain for certain groups during treatment. Nevertheless, these findings demonstrate music medicine is a low-touch, cost-effective way to manage patients' psychological well-being in the often stressful context of a cancer infusion clinic.

AFFILIATIONS

[1]Department of Oncology, Wayne State University School of Medicine, Detroit, MI
[2]Population Studies and Disparities Research Program, Karmanos Cancer Institute, Detroit, MI
[3]Tumor Biology and Microenvironment Research Program, Karmanos Cancer Institute, Detroit, MI

CORRESPONDING AUTHOR

Felicity W.K. Harper, PhD, Barbara Ann Karmanos Cancer Institute, 4100 John R, MM03CB, Detroit, MI 48201; e-mail: harperf@karmanos.org.

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AUTHOR CONTRIBUTIONS

Conception and design: Felicity W.K. Harper, Allison S. Heath, Seongho Kim, Elisabeth I. Heath
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Collection and assembly of data: Felicity W.K. Harper, Allison S. Heath, Tanina Foster Moore, Elisabeth I. Heath
Data analysis and interpretation: All authors
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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Using Music as a Tool for Distress Reduction During Cancer Chemotherapy Treatment

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Elisabeth I. Heath
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