MECHANISMS OF ACTIVE MUSIC ENGAGEMENT TO IMPROVE HEALTH OUTCOMES OF CHILDREN WITH CANCER AND PARENTS (PINPOINT)

ClinicalTrials.gov Identifier: NCT03085927

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Protocol Version: October 16, 2018

1.0 BACKGROUND & RATIONALE

Emotional distress in parents and their young child (ages 3-8) with cancer during acute treatment is a prevalent, persistent problem associated with physical symptom distress and diminished quality of life and family function.[1-7] In the longer term, this acute emotional distress is related to traumatic stress symptoms after treatment ends. As many as 58% of parents and 40% of childhood cancer survivors later report traumatic stress symptoms in the moderate to severe range.[1,2,8-13] These young children and parents require palliative care interventions to manage acute treatment distress and prevent secondary psychosocial morbidity, yet a recent systematic review revealed a glaring absence of empirically validated interventions for this age group.[14]

Music therapy, one of the most frequently used arts-based therapies, has become standard palliative care in many pediatric and adult hospitals; however, few studies have examined mechanisms by which music therapy works.[15-18] Music-based play is a pervasive, spontaneous, and normal aspect of family life that structures and supports meaningful interactions, and is a primary way young children cope with traumatic experiences.[19-27]

Based on Robb's music therapy theoretical framework, we developed and tested the Active Music Engagement (AME) intervention, establishing it as a feasible/acceptable intervention that reduces emotional distress in young children hospitalized for cancer treatment.[24,25,28] The music therapist-led AME uses music-based play and parent education/support (music play resource kit; tip sheets). The AME builds on existing skills, minimizing the burden of learning new skills during a stressful time when learning can be less efficient.[29] As parents witness intervention benefits for their child and learn how to use normalizing play activities to help manage their child's distress, traumatic reactions to and distressing memories of hospitalization may be minimized for both children and parents. The AME is particularly viable because it is easy to implement and teaches parents/children how to therapeutically use a familiar activity to manage distress.

As a palliative care intervention, the AME was developed to help manage distress and offer psychosocial support during acute cancer treatment. Three preliminary Active Music Engagement studies were conducted by our research team. **Study 1** was a descriptive study conducted to measure the presence/absence of contextual support (i.e., structure, autonomy support, relationship support) in the environment and levels of child engagement across three conditions (usual care, AME, and audio-storybooks). Findings indicated that the AME intervention: 1) was theoretically aligned with Robb's Contextual Support Model for Music Therapy (CSM-MT), and 2) engaged children significantly more than usual care or attention control conditions.[24]

Study 2 was a multi-site, non-randomized (sequential assignment) study that established feasibility/acceptability of a single-session, therapist-led AME intervention and audio-storybooks as an attention control condition. In this study we examined two attention control conditions (music listening and audio-storybooks). Music listening did not demonstrate any significant behavioral benefits and was not well accepted by parents. In contrast, the audio-storybooks condition was acceptable to parents but did not demonstrate any significant behavioral benefits, validating it as the best control condition for our current study. In addition, children randomized to the AME intervention demonstrated significantly more engagement behaviors than children in the control conditions (i.e., the proximal mediator proposed in this trial). [25]

Study 3 was a randomized pilot study that examined feasibility, acceptability, and preliminary efficacy of a parent implemented AME. In this study we translated the AME into a parent-led intervention and added parent instruction/coaching. Findings indicated the intervention and design were feasible, highly acceptable, demonstrated significantly more child engagement and parent child interaction behaviors, and produced positive outcomes for children. However, although parents were able to deliver the intervention they expressed: 1) preference for more therapist involvement/support during

scheduled sessions (i.e., therapist-led vs. parent-led sessions) in order to be more focused on their child; and 2) preference to have parent-led and/or child-initiated AME play between scheduled sessions. Parent interview data also supported child engagement, family normalcy, and parent self-efficacy as important potential mediators of intervention effects. Based on these studies, our team has established the AME as beneficial in managing child distress, and we have created a theoretically sound conceptual framework proposing mechanisms of action responsible for change in our targeted outcomes.[28]

These studies have positioned our team well for the current study, which will now test the mechanisms of action (proximal/distal mediators; moderators) proposed in our conceptual framework. We know from our prior studies that the proposed study design/procedures are feasible and acceptable, that the AME is theoretically aligned with the guiding conceptual framework, Robb's CSM-MT, and have preliminary effect size data about the relationship of the AME to our proposed proximal/distal mediators and outcomes.

2.0. OBJECTIVES AND SPECIFIC AIMS

The objectives of this two group randomized controlled trial is to identify behavioral, sociological, and psychological variables contributing to positive outcomes observed in previous AME studies (i.e., mediators) and identify for whom the intervention works (i.e., moderators). We will examine proximal mediators of child engagement and parent-child interaction and distal mediators of perceived family normalcy, parent confidence (self-efficacy) about their ability to support their child during treatment, and independent parent/child use of music play to manage distress during hospitalization. We hypothesize that these factors mediate change in outcomes of child emotional distress, physical symptom distress, and quality of life; parent emotional/traumatic distress and quality of life; and family function.[24,25,28,30] Published literature and our parent interview data support the proposed mechanisms of action; therefore, a mechanistic study of mediators and moderators of intervention effects is the next logical step.[28] In some instances we will consent the child's caregiver if they are currently fulfilling the role of the parent. Specific aims and hypotheses are to:

Aim 1: Examine the effects of proximal and distal mediators of the Active Music Engagement (AME) intervention on outcomes for young children with cancer and parents.

Hypothesis 1.1: Child engagement and parent-child interaction (proximal mediators) will mediate the effect of AME on perceived family normalcy, parent self-efficacy, and independent parent/child use of music play.

Hypothesis 1.2: Perceived family normalcy, parent self-efficacy, and independent parent/child use of music play (distal mediators) will mediate the effect of AME on child outcomes (emotional distress, quality of life), parent outcomes (emotional distress, traumatic distress, quality of life), and family function immediately post-intervention (Time 2) and 30 days post-intervention (Time 3).

Aim 2: Examine moderators of the AME intervention on outcomes for young child and parent distress.

Hypothesis 2.1: Child and parent distress with prior hospitalizations and child age will moderate intervention effects for child emotional distress and parent emotional/traumatic distress outcomes at Time 2 and Time 3.

Aim 3 (Exploratory): Explore child physical symptom distress in mediation and moderation models.

Hypothesis 3.1: Compared to attention control, children in the AME group will report less physical symptom distress (pain, fatigue, nausea) at Time 2 and Time 3.

Hypothesis 3.2: Perceived family normalcy, parent self-efficacy, and independent parent/child use of music play (distal mediators) will mediate the effect of AME on child physical symptom distress at Time 2 and Time 3.

Hypothesis 3.3: Child and parent distress with prior hospitalizations and child age will moderate intervention effects for child physical symptom distress at Time 2 and Time 3.

Findings will inform CSM-MT refinement and the use of music to manage treatment distress in other pediatric populations. Subsequent trials will examine AME cumulative effect across repeated admissions to manage distress and prevent traumatic stress symptoms in survivorship.

3.0. SAMPLE ELIGIBLITY CRITERIA

Child/Parent Inclusion Criteria and Rationale: Children and parents/caregivers will be eligible if: 1) the child is 3 – 8 years of age at time of enrollment (intervention content is not age-appropriate for other children); 2) patients with an expected treatment course of at least 3 days to receive moderate to high intensity chemotherapy and/or radiation therapy either in-patient or outpatient (children receiving chemotherapy are at risk for high symptom distress; 3-day treatment course is required to deliver study conditions and contributes to sample homogeneity); and 3) one parent/caregiver ($\geq$18 years of age) can be present for all sessions (study targets both child and parent/caregiver).

Child/Parent Exclusion Criteria and Rationale: Children and parents/caregivers will be excluded if: 1) the child and/or parent/caregiver do not speak English or 2) the child has a significant cognitive impairment that might hinder participation (determination made in consultation with attending physician, oncologist, and parents).

Sample Size. We will recruit a total sample size of 184 child and parent/caregiver dyads (368 total) and assume 15% attrition in order to retain 156 child and parent/caregiver dyads (78 dyads/group) at Time 3.

4.0. PARTICIPANT RECRUITMENT AND ENROLLMENT

Procedures mirror successful strategies used in Preliminary Study 3, and our current R01 music intervention study for adolescents/young adults undergoing high risk cancer treatment and their parent.

Recruitment & Informed Consent. The recruitment and informed consent procedures will preserve participants' right to refuse and guarantees that potential subjects who refuse will not be known to the research team. Children and parents/caregivers will be recruited from Riley Hospital for Children, Children's Mercy Hospital, Children's Healthcare of Atlanta, and University of Texas MD Anderson Cancer Center during clinic visits. As with our previous and current studies, the hematology/oncology coordinators, who will not be employed on the study, will identify potentially eligible parents/ caregivers and children using an eligibility checklist. The coordinators then meet with potentially eligible parents/children to provide an initial study introduction, verify eligibility, and provide a study brochure. After the coordinators gain parent/patient approval, the coordinators will contact the project manager/PI to make contact with the parent/patient. The PI or project manager will contact the interested child/parent, explain the study, randomization procedures, intervention schedule, and assess willingness to participate. Written parent/caregiver consent for self and their child, and assent for children > 6 years will be obtained, following the requirements of the human subjects review committee. The hematology/oncology coordinators are nurses who are trained and employed to enroll children/parents on clinical trials for their respective programs. We have worked closely with them on our previous and current studies with great success.

Data Collection & Randomization Procedures. Following consent, the project manager will arrange a time for parents/caregivers to complete baseline (T1) measures during a routine clinic visit, prior to their next scheduled chemotherapy admission. A trained evaluator will administer measures in a quiet/private setting and remain available for questions. The child/parent or caregiver dyad will then be stratified by child age (preschoolers 3-5 years; school-agers 6-8 years) and randomized in blocks of six to the AME or attention control condition by our statistician. After the PI or project manager from the enrolling site receives randomization status from our study statistician, she will inform the parent/child of their randomization status and will then immediately schedule Session 1. Only the

project manager, PI, statistician, and intervener will know the child/parent dyad's randomization status. Evaluators will be blinded.

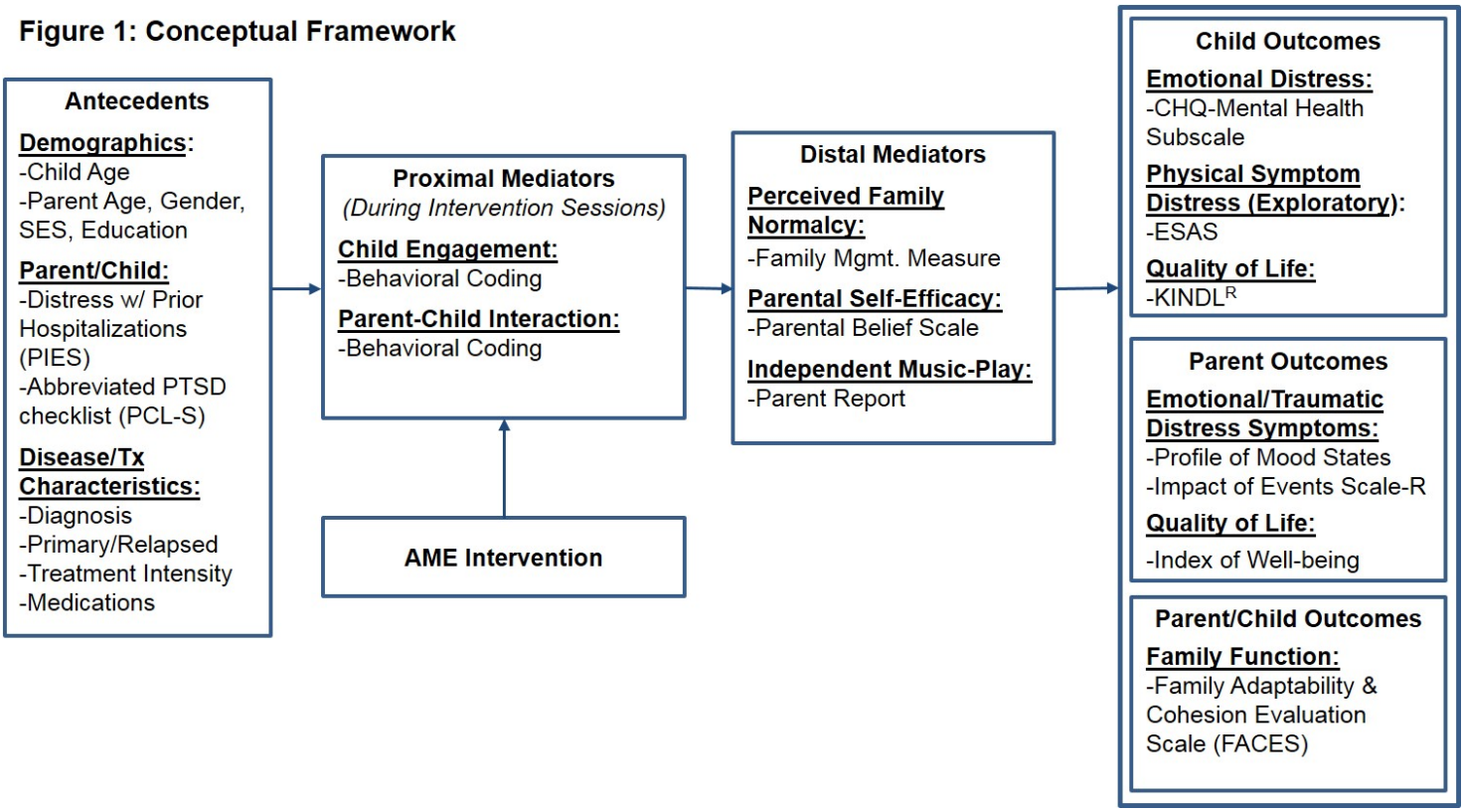
All study condition sessions will be video recorded to facilitate collection of child engagement and parent-child interaction data and monitor treatment fidelity. Sessions 1 and 2 are video recorded to desensitize children/parents to video recording; only Session 3 video data are analyzed for Aim 1. In our previous studies, video recording did not negatively affect participant accrual. An evaluator, blind to randomization status, will administer T2 measures after Session 3. Evaluators will administer T3 measures 30 days (+/- 7 days) post-intervention during a subsequent clinic visit or by telephone. Parent self-reports will be used to monitor use of study condition activities between sessions and between T2 and T3 data collections (Appendix 1).

5.0. RESEARCH DESIGN, METHODS, AND PROCEDURES

Conceptual Framework. Our conceptual framework (Figure 1) is based on Robb's Contextual Support Model of Music Therapy[24,30] and further informed by Kazak's Pediatric Medical Traumatic Stress Model,[4] which provides a useful heuristic for understanding short and long-term consequences of pediatric cancer treatment for parents and their child. In our conceptual framework, recurring events related to cancer treatment (i.e., hospitalizations, procedures) are viewed as potentially traumatic events. Parent appraisal of events as traumatic or not traumatic is influenced by pre-existing factors, which serve as antecedents in our study.

Published research indicates that higher parent and child distress during cancer treatment and survivorship is related to: 1) demographics (younger child/parent age, female parent gender, and lower socio-economic status/education),[36,37] 2) higher parent/child distress with prior hospitalizations, and greater traumatic stress symptoms,[1,2,38] and 3) disease and treatment characteristics (diagnosis, relapsed disease, greater treatment intensity).[5,10,12,13,39]

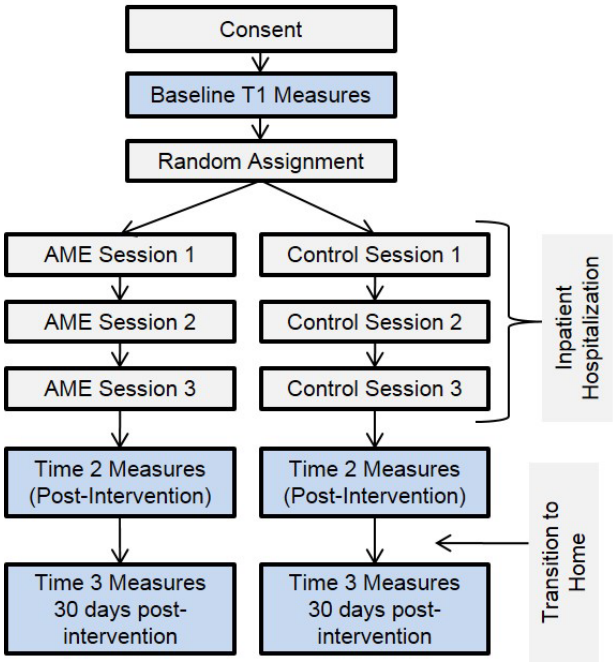
Figure 1: Conceptual Framework



The AME directly targets the proximal mediators of child engagement and parent-child interaction,[24,28] as well as distal mediators of perceived family normalcy,[40] parent confidence (self-efficacy) about their ability to support their child during treatment,[41] and independent music play between therapist-led sessions.

Our study examines proximal and distal mediators of the AME on outcomes for young children (emotional distress, physical symptom distress (exploratory), quality of life), parents (emotional distress, traumatic distress, quality of life), and family function. In addition, we examine moderators of the AME intervention on outcomes (child/parent distress with prior hospitalizations; child age). This study will allow us to determine *how* and *for whom* the intervention works, informing a subsequent trial to examine cumulative impact/efficacy of AME across repeated cancer treatment admissions to manage distress and prevent traumatic stress symptoms in survivorship. Findings will also have implications for use of the CSM-MT to guide development of active music interventions to manage treatment distress in other populations.

Study Design. This is a two-group, randomized, controlled trial. Children and one parent will be stratified and randomized in blocks of six to the AME intervention or attention control condition (see Study Schema). Child/parent dyads will be stratified by child age (preschoolers 3-5 yrs; school-agers 6-8 yrs). Both conditions are standardized and each group will receive three 45-minute sessions over 3 days. We chose a randomized, controlled trial over a single-group trial as a control group is optimal for ruling out confounding variables that may impact the relationships between the intervention, mediators, and outcomes. For example, a single-group trial requires a dose be measured to represent the intervention since the variable being mediated must have some variation. The dose may be impacted by several unknown factors that could make interpretation of results difficult.[55] Our prior studies suggest that 1) a usual care condition would likely have high attrition and negatively affect study accrual, and 2) our audio-storybooks low dose condition was acceptable without behavioral benefits. Thus, we will use audio-storybooks as our attention control condition. The number of sessions and amount of contact time were selected based on average length of stay and findings from our preliminary studies which found immediate and longer-term (30 days post-intervention) benefit.[24,25,28]



As in our preliminary studies, baseline data (Time 1) will be collected after consent. Time 2 data are collected post-Session 3. Parents/children are encouraged to use AME and low dose audio-storybooks activities between sessions and at home following discharge and self-reported frequency and duration of activities will be collected during sessions 2 and 3, and at T3 (30 days post-intervention). Data collection timelines are based on positive findings from our preliminary studies and inform our primary aims which examine mediation. Findings will inform a subsequent trial to examine long term benefits. See Study Schema for assessment timelines.

Setting. Young children (ages 3-8 years) and their parents will be recruited from three children's hospitals. These hospitals are in metropolitan areas that serve large catchment areas. All three sites are members of the Children's Oncology Group, which treats similar types of cancer diagnoses with similar therapeutic protocols. The inpatient hospital setting and outpatient hematology/oncology clinic will be used for delivery of intervention and attention control conditions; data collection will occur both in the clinic and in-patient setting. All sites have verified availability of dedicated, private space for these activities.

Study Procedures. Procedures mirror successful strategies used in Preliminary Study 3, and our current R01 music intervention study for adolescents/young adults undergoing high risk cancer treatment and their parent.

Recruitment & Consent. Children/parents will be recruited during a clinic visit. As with our previous/current studies, certified research coordinators will use the eligibility checklist to identify potential participants and notify the project manager. The project manager will then contact the child/parent, explain the study, and if they are interested, obtain written parent consent for themselves and their child and assent for children > 6 years, following human subjects review committee requirements.

Data Collection & Randomization Procedures. Following consent, the project manager will arrange a time for parents to complete baseline (T1) measures during a routine clinic visit, prior to their next scheduled chemotherapy admission. A trained evaluator will administer measures in a quiet/private setting and remain available for questions. The child/parent dyad will then be stratified by child age (preschoolers 3-5 years; school-agers 6-8 years) and randomized in blocks of six to the AME or attention control condition by our statistician. The PI or project manager will then immediately schedule Session 1. Only the project manager, PI, statistician, and intervener will know the child/parent dyad's randomization status. Evaluators will be blinded.

All study condition sessions will be video recorded to facilitate collection of child engagement and parent-child interaction data and monitor treatment fidelity. Sessions 1 and 2 are video recorded to desensitize children/parents to video recording; only Session 3 video data are analyzed for Aim 1. In our previous studies, video recording did not negatively affect participant accrual. An evaluator, blind to randomization status, will administer T2 measures after Session 3. Evaluators will administer T3 measures 30 days (+/- 7 days) post-intervention during a subsequent clinic visit or by telephone. Parent self-reports will be used to monitor use of study condition activities between sessions and between T2 and T3 data collections (Appendix 1).

Study Condition Procedures. Consistent with our other studies, we train music therapists to deliver both intervention and control conditions to minimize risk for unblinding evaluators to participant group assignment. Risk for experimental drift, bias, and diffusion will be addressed through four quality assurance monitoring procedures established in our previous trials.[56] Children/parents randomly assigned to AME or attention control receive the same length of sessions (45 min.) and timing of contact (3 sessions, 3 consecutive days). Session 1 will occur within 24 hours of hospital admission.

Usual care at all three sites. Across all sites, chemotherapy is administered according to Children's Oncology Group protocol guidelines, ensuring consistency of treatment. Antiemetic regimens are similar across sites and tailored to patient-specific needs. We will document patient medications at baseline, during hospitalization (T2), and 30 days post-intervention (T3) and control for site in all analytic models.

Procedures. Following consent, the project manager will arrange a time for the parent to complete baseline measures during a routine clinic visit, prior to their next scheduled chemotherapy admission. Baseline measures will be completed in a private room in the outpatient clinic. A trained evaluator will administer the baseline measures and remain available for questions during measurement completion. The evaluator will immediately notify the project manager that baseline measures are completed. The child/parent dyad will then be randomly assigned to the AME or the attention control condition by the study statistician. The PI or project manager will then immediately notify the child/parent of their randomization status and schedule their first session with the intervener. Only the project manager, PI, statistician, and intervener will know the child/parent's randomization status.

AME Intervention. Parents/children randomly assigned to the AME intervention receive three, 45-minute sessions with the music therapist, delivered daily, for 3 consecutive days. Session 1 is delivered within 24 hours of hospital admission. AME intervention sessions are designed for delivery by a board-certified music therapist (MT-BC) who tailors music-based play experiences to encourage active engagement in and independent use of music play as a strategy to manage distress. During AME sessions, the music therapist provides children/parents repeated opportunities to experience competence, autonomy, and meaningful interactions through music-based play activities, and

provides support/education about ways music play can be used to manage distress and sustain a sense of family normalcy while hospitalized and as they transition home.

There are three components to the AME intervention: 1) therapist-led music-based play activities and sessions, 2) the music play resource kit (to promote independent music play), and 3) tip sheets for parent education and support that focus on why music play, how to use music play during hospitalization, and how to use music play during transition from hospital to home. During each session, the music therapist begins with a 5 minute introduction/assessment period, followed by a 30 minute music play session, and closes with a 10 minutes of parent education and tailored suggestions for using music play outside sessions.

The child/parent also receive a music play resource kit to use during and between therapist-led sessions. The kit includes: 1) a professional CD recording of music composed and/or arranged specifically for this project, 2) age-appropriate musical instruments and play materials that correspond with each activity, and 3) activity cards designed to give children/parents at-a-glance information on ways they can use their kit. Universal precautions and hospital sterilization protocols will be observed for the compact disc players, compact disc recordings, music play resource kits, and other study materials. Children receive their own music play resource kit to keep both during and after study completion.

Attention Control (Audio-storybooks). Parents/children randomly assigned to the audio-storybooks attention control condition will have the same length of sessions (45 minutes) and timing of contact (3 sessions, 3 consecutive days) as the AME intervention group. Session 1 is delivered within 24 hours of hospital admission. The audio-storybooks (ASB) condition is designed to control for attention from an intervener, shared parent-child experiences, and audio-visual stimulation. It offers parents/children opportunities to make choices and engage in an age-appropriate, non-music-based play activity. In each session children/parents will choose and listen to one of two illustrated children's books with audio-taped narration. Children/parents receive a kit that includes 3 audio-storybooks that they can keep. Universal precautions and hospital sterilization protocol will be observed for the compact disc players, compact disc recordings, audio-storybooks kit, and other study materials. Children receive their own audio-storybooks kit to keep both during and after study completion.

All study condition sessions will be video recorded to facilitate collection of behavioral outcome data and monitor treatment fidelity. Sessions 1 and 2 are video recorded to desensitize children/parents to video recording; only Session 3 video data are analyzed for Aims 1 and 2. In our previous studies, video recording did not negatively affect participant accrual or cause distress. An evaluator, blind to randomization status, will administer T2 measures after Session 3. Evaluators administer T3 measures 30 days (+/- 7 days) post-intervention during a subsequent clinic visit or by telephone. All evaluation sessions are audio-recorded to monitor evaluation fidelity.

Treatment Fidelity Strategies. Our team developed and published treatment fidelity strategies consistent with NIH Treatment Fidelity Workgroup recommendations to ensure treatment integrity, minimize experimental drift, and minimize contamination of the control group.[56,57] Strategies include: 1) standardized intervention and control condition protocols, study manuals, and training; 2) self- and external monitoring of video-recorded intervention/attention control sessions; 3) self- and external monitoring of audio-recorded evaluation sessions; 4) quality assurance checklists to track protocol deviations; 5) intervener field notes to document duration and frequency (dose), and uptake of study conditions; 6) separate intervener/evaluator conference calls; and 7) weekly study administration team meetings to address any concerns.

Sources of Materials. All data will be collected solely for the purposes of this study. Parents will complete a set of study measures three times (baseline, post-session 3, and 30-days post-session 3). We estimate it will take the parent 30 – 45 minutes to complete measures.

All measures will be completed using paper/pencil administration. Once parents complete a set of measures our evaluators will directly enter data into RedCap, a HIPAA compliant web-based data

management system. Paper measures will be secured in a locked cabinet, in a locked office dedicated to our study.

Medical information will be obtained from chart reviews, relevant to diagnosis and treatments. These data will be obtained by our evaluators, all of whom are Children's Oncology Group Certified Research Associates.

Field notes on intervention and evaluation sessions will be completed by music therapist and evaluators using a password protected computers that are connected to a secure web-based server. All study related materials and forms are stored on HIPAA compliant encrypted data management server.

All intervention and attention control sessions will be video recorded, and all evaluation sessions audio recorded to facilitate collection of behavioral outcome data and to monitor fidelity.

A listing of specific measures can be found in Section B and in Appendix 1 of this application. Only the PI and the project coordinator will have access to subject identities; all raw data, including digital audio and video data will be stored according to Indiana University IRB requirements.

Potential Risks. Risks to child/parent participants are considered minimal and include: 1) breach of confidentiality; 2) increased fatigue for the child or parent as a result of participating in study session activities or completing measures; and 3) psychological discomfort for the parent when responding to evaluation questions.

Protection Against Risk

Confidentiality. To minimize the possibility that a breach in confidentiality will occur, data for this study will be kept separate from any subject identifiers and will be kept in a locked file cabinet and on a secure, encrypted data management server. Digital audio and video recordings of child/parent participation in study sessions will also be uploaded on a secure, password protected computer server that is backed up by the university's main computer system. Only the PI, Co-I, PM, and designated research assistants will have access to the data. Computers where data will be entered will be accessed through passwords and kept in locked offices. Data monitoring will occur in three stages: 1) field editing for missing data by evaluators; 2) office editing by a designated research assistant after instruments are returned to the office; and 3) listening to random samples of 25% of the audio-taped evaluation sessions and video-taped intervention sessions by the PI or Co-I.

Fatigue. Interveners and evaluators will be trained to observe for increasing fatigue and ask parents' to indicate if the child's or their own fatigue is at a level where the activity should be stopped. Also, intervention sessions or control condition sessions, and evaluations will be stopped if the intervener or evaluator assesses a level of fatigue in the child or parent that precludes their ability to participate. Children and parents will be informed they can stop the session at any time and/or stop their involvement in the study at any time.

Psychological Discomfort. Interveners and evaluators will receive specific training in identifying and responding to psychological discomfort related to group assignment and to evaluation. Parents and children will be informed they can stop the session at any time and/or stop their involvement in the study if they become uncomfortable. Should psychological discomfort be identified, a protocol will be in place to notify the PI. The attending oncologist and nurse on the unit will also be notified of the concern in order to make a decision regarding referral. The PI or Project Manager will follow up within 24 hours on decisions made. Should any child give any indication the level of psychological distress is at a level of danger to self or others, the child's parent and attending oncologist will be immediately consulted to arrange an evaluation at Riley Hospital (Indianapolis site), Children's Mercy Hospital (Kansas City site), Children's Healthcare of Atlanta (Atlanta site), or University of Texas MD Anderson Cancer Center (Houston site) unless the parent indicates a preference for treatment elsewhere. In the event that a parent is judged to be a danger to self or others, the child's primary care oncologist will be consulted to arrange an evaluation, unless the parent indicates a preference for treatment

elsewhere. Again, parents and children will be informed they can stop the session at any time and/or stop their involvement in the study at any time.

6.0. MEASURES AND DATA COLLECTION INSTRUMENTS

All measures reflect careful consideration of psychometric properties, sensitivity to change, and response burden.[24,25,58-70] See Appendix 1 for measures and additional psychometrics.

Variable(s)	Measure	# Items	Reliability Evidence	Admin. Schedule	Completed By
Antecedent Factors					
Demographics *-parent/child age, parent gender, SES, parent education*	Family Information Form	3	N/A	T1	Parent
Prior Distress w/ Hospitalization *-parent/child*	Prior Illness Experiences Scale (PIES) Abbreviated PTSD checklist (PCL-S)	13 6	.78† .94†	T1 T1, T2, T3	Parent Parent
Disease Characteristics Treatment Characteristics	Diagnosis and Treatment Form Intensity of Treatment Rating Scale Medication Data Form	2 1 7	N/A .95* N/A	T3 T3 T1, T2, T3	Evaluator Oncologist Evaluator
Proximal Mediators					
Child Engagement Parent-Child Interaction	Behavioral Coding Form Behavioral Coding Form	N/A N/A	.85* 85*	Session 3 Session 3	Trained Coder Trained Coder
Distal Mediators					
Family Normalcy Perspective	Family Management Measure (FaMM) *Family Life Difficulty Subscale*	14	.90†	T1,T2,T3	Parent
Parent Self-Efficacy	Parental Beliefs Scale (PBS)	20	.85†	T1,T2,T3	Parent
Independent Music Play	Parent Report	2	N/A	Sessions 2/3; T2	Parent
Child Outcomes					
Child Emotional Distress	CHQ – *Mental Health Subscale*	16	.81†	T2, T3	Parent
Child Physical Symptom Distress	Edmonton Symptom Assessment System (ESAS)	3	.69-.80†	T1, T2, T3	Parent
Child Quality of Life	KINDL^R	20	.89†	T1, T2, T3	Parent
Parent Outcomes					
Parent Emotional and Traumatic Stress Symptoms	Profile of Mood States-Short Form (POMS) Impact of Events Scale-Revised (IES-R)	37 22	.99** .84-.91†	T1,T2,T3 T1, T2, T3	Parent Parent
Parent Quality of Life	Index of Well-being	9	.93†	T1, T2, T3	Parent
Parent/Child Outcomes					
Family Function	(FACES II)	30	.90†	T1,T2,T3	Parent

†Cronbach's alpha; *inter-rater reliability; **correlation with POMS

7.0. STATISTICAL CONSIDERATIONS

As part of Preliminary Study 3, we have already created and successfully implemented a secure web-based system to capture the study data using the REDCap database management system, as well as a telephone log system and participant calendar that will enable the research coordinators to track and schedule participants' visits. We will review and process data using already-programmed multiple verification and edit-checking programs. We will also conduct rudimentary analyses to ensure that the data have been properly collected and to identify any outliers or errors.

Preliminary analyses: Prior to hypothesis testing, we will calculate coefficient alpha as a measure of internal consistency reliability on all multiple-item scales. Construct validity will be assessed by calculating Pearson or Spearman correlations between scales to determine if correlations are in the expected direction. We will assess multicollinearity between the scales for the mediators by examining the correlations above. If any pairwise correlations are 0.7 or higher we will not include both variables in a given model but fit separate models instead and acknowledge this issue in the interpretation. We will also compare the AME group to the attention control group with respect to demographic and baseline outcome variables using two-sample *t* tests, chi-square tests, or Fisher's

Exact tests as appropriate. We will control for any demographic variables that are not balanced in the models below (all models will adjust for baseline outcome). We will also control for site in all models.

Main analyses: For analyses below we will analyze as randomized and attempt to collect outcome data on non-completers, following the intent-to-treat principle. For Aims 1 and 2, each outcome will be modeled separately. Also we will model T2 separately from T3. Thus, there will be a total of 12 models in Aim 1 (6 outcomes x two time points). In Aim 2, two outcomes will be examined and 3 potential moderators at two time points for a total of 12 (2 outcomes x 3 moderators x 2 time points) models. For Aim 1, our primary goal is to test mediation effects. Mediation effects will be estimated in an ANCOVA setting, fitting the appropriate mediation models using MPlus[71] and then testing indirect effects using the percentile bootstrap approach to estimate the indirect effect.[35] The multiple mediation model with three-path mediation effects specifies that the intervention will act through the proximal and distal mediator on the outcome and also have a direct effect on the outcome. Each outcome model will have 6 key predictors (intervention, two proximal mediators, 3 distal mediators), and control for T1, age (3-5 years vs. 6-8 years), site, and any imbalanced baseline covariates found above (allowing for up to 6 imbalances). Thus we will have up to 15 variables in any model. For Aim 2, we will test moderation effects by including the appropriate interaction terms of the potential moderator (dichotomized at the median) with the intervention indicator (AME vs. attention control) in our models. For all models in Aims 1 and 2, we will assess goodness-of-fit (GOF) using standard GOF measures (comparative fit index, root mean square error of approximation, and root mean square residual). For Aim 3, an exploratory aim, we will use ANCOVA to compare changes in child symptom distress at T2 and T3 between intervention and control groups. In light of positive findings, we next will explore models as in Aims 1 and 2 to assess for potential mediation and moderation effects for this outcome.

Missing data and multiple comparisons: We will compare all baseline variables between subjects who drop out of the study and those who do not using two-sample *t* tests, chi-square tests, or their non-parametric equivalents as appropriate. MPLUS software will incorporate participants who drop out before completion by using the MPLUS imputation method to perform a bias adjustment for missing data under maximum likelihood estimation and the assumption that data are missing at random. If we find that missing data are not missing at random, we will use a pattern mixture modeling approach to address; however, based on our prior studies we expect limited attrition (<15%) and little to no missing data on instruments (<1%). As our primary outcomes are child (CHQ) and parent emotional/traumatic (POMS) distress and other outcomes are considered secondary, we do not plan on adjusting *p* value for multiple comparisons for the primary outcomes but will apply the Hochberg step-up procedure for the secondary outcomes.

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