The following protocol information is provided solely to describe how the authors conducted the research underlying the published report associated with the following article:

Specificity of Problem-Solving Skills Training in Mothers of Children Newly Diagnosed with Cancer: Results of a Multisite Randomized Clinical Trial

Sahler, et al

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Maternal Problem-Solving Skills Training Redacted Protocol

Original Protocol (note modification in 11/06)

Selection of Participants

Eligibility Criteria

Subjects will be drawn from the pool of all mothers who are primary caregivers of children diagnosed with any form of cancer 2-16 weeks prior to contact about the PSST intervention and cared for at one of the 5 data collection sites (dense sampling). No attempt will be made to stratify the sample by any particular demographic variables (e.g. age, ethnic background, or type of cancer diagnosed in their child), except that monolingual Spanish-speaking mothers will be specifically recruited to provide adequate representation for statistical analysis.

Gender Restriction

To control for gender differences in negative affectivity only mothers will be included.[49-50] Furthermore, because both the richest literature and our own data on parental coping have been based on studies of mothers, we believe maternal data will be most reliable and comparable.

Diagnosis Restriction

None. Accepting mothers of children with any form of cancer increases generalizability.

Exclusionary Criteria

Mothers of children with cancer will be excluded from the project if (1) they do not read or speak English or Spanish; (2) their child is in severe a medical crisis, as determined by the oncologist or (3) they live a prohibitive distance to complete the intervention (typically, > 50 miles from the Center).

Medical Stability Requirement

We will recruit mothers of children undergoing induction therapy. Mothers with children in acute medical crisis are specifically excluded. That is, until the curriculum materials are of such proven efficacy that virtually any family could benefit from such instruction, we do not feel justified in asking mothers dealing with acute or continuing medical crises to commit the level of energy necessary to engage effectively in materials development. Thus, we are seeking a sample that we think will not only benefit from the experience but also be able to help in refine PSST for wider applicability.

Distance from Center Requirement

This is for convenience. The project requires mothers to provide data on 3 occasions and to participate in 8 training sessions. Although these visits will coincide with patient hospitalizations or outpatient visits whenever possible, some sessions may be scheduled at other times or require a home visit. The distance-from-Center requirement increases the likelihood of successful participation.

Non-Participants

A list of possible participants with reasons why they were not approached (e.g., scheduling problems) will be maintained and submitted to the data coordinating site each month. A contact form with minimal demographic information and reasons for non-participation will be submitted for each mother approached to allow us to calculate refusal rates and describe the population of non-participants.

Terms of Participation and Incentives

Each potential participant will receive a written description of the study, its goals, and the randomization procedure. Those who agree to participate will sign an informed consent document outlining the nature and duration of participation as approved by the Institutional Review Board of the Center at which her child receives care. Each individual who agrees to participate will complete a 1-hour baseline (T^1) assessment prior to randomization. Specific learning objectives and outcome measures for each session are included in the PSST Parent Handbook given to those who are randomized into one of the PSST instruction groups. The immediate post (T^2 10-12 weeks) and 3-month post (T^3 weeks 17-23) evaluations will be conducted as additional sessions. Each subject will receive a stipend of $50 when the T^3 assessment is completed.

Recruitment

Every *nth* mother of a newly diagnosed child with cancer will be approached regarding participation, where *n*=# new diagnoses per year/# subjects to be recruited per year divided by 2 (assuming a 50% recruitment rate, which, from our past experience [70%-90%], is conservative). Recruitment, which will occur between 2 and 16 weeks, is typically conducted during induction or the first few outpatient treatment visits. The

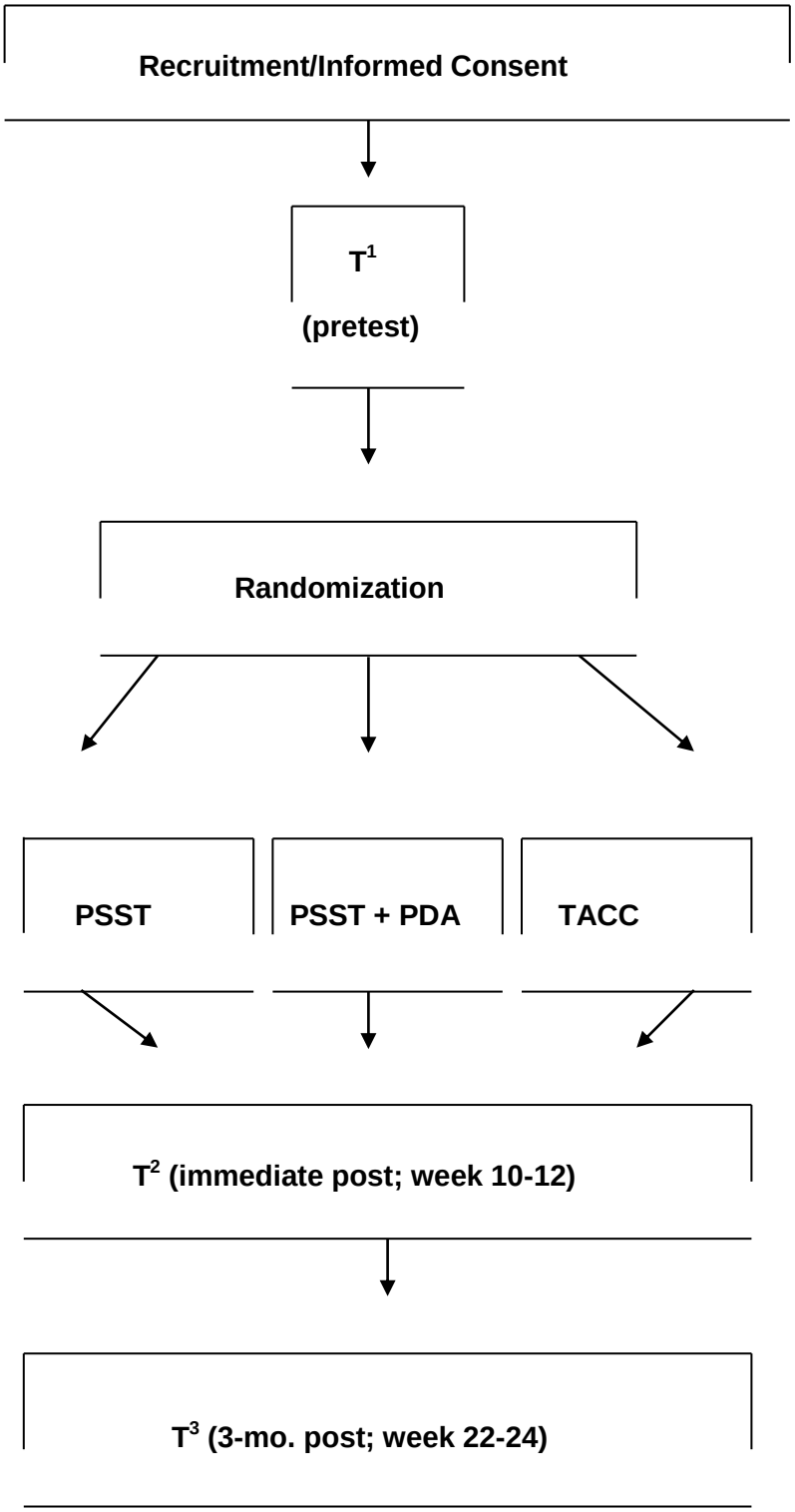
specific recruitment routine varies by institution depending on usual practice for subject recruitment, but will be approved by each individual Human Subjects Review Board.

Our experience has been that English-speaking mothers are more likely to agree virtually immediately, whereas Spanish-speaking mothers require greater outreach. Recruitment is typically accomplished through direct contact by the RA, using the appropriate language, after ascertaining that a particular mother meets the eligibility criteria. The intervention is explained to family members at a mother's request. Every effort is made to assure full and complete participation including follow-up phone calls, flexible scheduling, assisting with transportation, and home visits, if needed.

Randomization Procedures

Randomization will occur centrally upon receipt of eligibility data from a participating institution. The process begins at the individual sites. After ascertaining eligibility and obtaining consent, pertinent registration information will be entered through an Internet site at the Data Management Center (DMC). To insure confidentiality, a login ID and password will be required. Registration information will not include the participant's full name, but will contain sufficient information to uniquely identify the subject. Allocation of subjects to intervention groups will be balanced within each institution and within strata defined by language. A back-up procedure will be in place in the rare event that internet communications fail for a 24-hour period.

Schema and Treatment Plan:



Interventions

PSST

This intervention will consist of eight 1-hour in-person sessions conducted at the hospital, the clinic, or the mother's home, or by telephone according to the manual and parent's guide developed for our earlier studies.

TACC

To determine which aspects of PSST efficacy are due to non-specific intervention effects of time, attention, and social support, a time-and-attention control condition (TACC) is proposed as an arm of the current study. Subjects randomized to TACC will receive eight 1-hour in-person sessions with the research assistant.

Although the PSST intervention and the TACC intervention ("reflective listening", see below) are very different therapeutic techniques and will be delivered by different RAs, there is certainly some element of reflection inherent in any psychotherapeutic contact. It is vitally important, however, that no PSST be described during a TACC session. Thus, detailed guidelines for the TACC will be developed and will be contained in a TACC treatment manual. The role of the Treatment Integrity element of the proposed project (see below) is to ensure maximum separation between the interventions.

Rationale for a TACC: Crits-Christoph[60] argues for the inclusion of a control group in psychotherapy research studies, as it appears necessary to adequately control for major nonspecific factors. He suggests that a "reflective listening" approach is very appropriate for such studies. One study in which an alternative treatment condition was used to control for nonspecific effects was by Borkovec and Costello.[61] They used a "reflective listening" non-directive approach as a comparison condition to cognitive-behavioral treatment for generalized anxiety disorder. Subjects were also asked to rate the two approaches on constructs such as credibility, expectations, and the therapeutic alliance. Results yielded poorer outcomes for the reflective listening condition as compared with cognitive-behavioral treatment, with an effect size of .90 (Cohen's *d*). Nevertheless, subjects rated the reflective listening treatment as "equal in credibility, expectations for improvement, and quality of the therapeutic alliance to cognitive-behavioral treatment." For the purposes of the present study, the clinical appropriateness of reflective listening, along with empirical documentation of its therapeutic non-specific effects, is key to our choosing it as our TACC.

For our TACC, we plan to use a "reflective listening" approach patterned after Rogers' Person-Centered Approach in Client-Centered Therapy.[62] We will use a modified version because of the time-limited nature of this study and the necessity of having research assistants conduct the therapy. The fundamental elements of this intervention

will include: (1). The RA will take a non-directive approach and refrain from direct suggestions or instructions; (2). The RA will provide restatements and summaries of what the subject has said, literal responses to direct questions, statements that point toward the felt experience of the client, and questions that convey understanding of the subject's expressed ambiguities. Empathic understanding will be the goal for this approach; (3). When asked, the RA may answer questions, give explanations, and encourage the subject to find and use resources that will be helpful; and (4). Session content will derive from subjects' priorities and needs at the time and will not focus on any specific skills training. In particular, concepts, principles, and techniques of PSST will be avoided per manual directions and RA training and supervision.

Thus, the basic techniques in the TACC will include active listening, reflection of feelings, clarification, and "being there" for the subject. The RA will listen to what the subject is saying, check that understanding with the client if it is not clear, and treat the client with the utmost respect and regard. The focus will be on the present moment and on experiencing and expressing feelings. According to Rogers,[62] his approach is well suited for the initial phases of working with clients in crisis, and it is useful as well for working with groups composed of people from diverse cultural backgrounds.

The investigators in this collaborative group are senior clinicians with backgrounds in Clinical Psychology and Behavioral Pediatrics and extensive experience in psychosocial interventions, especially in pediatric psycho-oncology. In addition, all have trained clinicians in a variety of techniques including reflective listening, a backbone of supportive psychosocial care. They will serve as the trainers for both PSST and TACC during the RA orientation and training meeting late in Year 1 of the project.

PSST + PDA

This intervention will consist of the eight 1-hour in-person sessions supplemented by a personal digital assistant (PDA) device that includes programs designed to provide: (a) a brief review of problem-solving; (b) review and practice of each of the five elements of the Bright IDEAS problem-solving approach; (c) prompts to use problem-solving skills; and (d) a periodic (e.g., daily) log to record problems confronted by the mother and her solutions. Between sessions, the subjects in this study arm will have unlimited access to this interactive, audio-visually enhanced technology-based educational tool. Elements of *Carmen's Bright IDEAS,* an artificial intelligence-based animation that explains and exemplifies PSST, was developed by the Information Systems Institute during a previous project and will be incorporated into the instructional programming. Thus, selected portions of the animated character's explanation of Bright IDEAS as well as illustrations and worksheets will be culled from the CD and loaded onto the PDA in both English and Spanish formats. PDAs will be loaned to mothers for the duration of their participation to ensure accessibility. Non-study-related functions will be disabled to increase the probability equipment will be returned. Additionally, the PC-based CD

version of Bright IDEAS will continue to be available to participants as adjunctive learning material during sessions just as it has in the past. Translation into Spanish text is easily achieved. Animated sections requiring lip-synching will be translated during the first several months of the project

The primary function of the PDA is to prompt adaptive behavior. For example, prompts such as "What is the problem?", "What are some alternative solutions?", "Try it out.", and then, at the next scheduled interaction, the question, "How did it work out?" might be asked. At this subsequent prompt from the PDA, the participant might be given encouragement to try other possible solutions from a menu of tailored strategies. Thus, this approach seamlessly integrates education with tailored PSST intervention prompts from the PDA. PDA technology can also measure adherence to daily monitoring by recording the time and day of each data entry. Additionally, PDA technology can record whether a participant accessed optional problem-solving tips. Thus, similar to blood glucose monitoring devices for individuals with diabetes, auditing usage via weekly downloading of data by the RA, allows us to determine whether/how often the mother used the PDA device for information on how to problem-solve challenges encountered in her daily life.

Rules for Dose Modification N/A

Measurement of Treatment Effect

Demographic Information

This will include information about the child with cancer, including age, diagnosis and date of diagnosis, maternal age, marital status, and educational level.

Acculturation

(Spanish-speaking subjects only) The 18-item Immigrant Stress subscale of the Hispanic Stress Inventory will be administered to learners and controls in the Spanish-speaking cohort.[51-52] This inventory was constructed in English and translated into Spanish according to recommended translation-back translation procedures. It has acceptable reliability and validity within the Hispanic population. The inventory assesses culturally specific stressful life conditions among adult Hispanic immigrants. The alpha coefficient is .85, and the test-retest coefficient is .80.

Problem Solving

The Social Problem-Solving Inventory-Revised (SPSI-R) [42,53-54] is a 52-item self-report instrument that is linked to a five-dimensional model of social problem-solving which, in turn, is derived from a factor analytic study of the original 70-item The SPSI-R consists of five scales that measure two different problem orientation dimensions (Positive and Negative) and three different problem-solving proper dimensions (Rational Problem-Solving; Impulsivity/Carelessness Style; and Avoidance Style). The SPSI-R is characterized by strong reliability and validity estimates.

Problem-Solving Vignettes. As an independent measure of problem-solving skills, defined as the ability to apply the essential steps in PSST, a series of 12 vignettes reflecting problem situations relevant to mothers of newly diagnosed children with cancer will be developed. This measure will be modeled after the Problem-Solving Task for Cancer (PST-C) developed by Maguth-Nezu and Nezu based on earlier versions used in their studies of PSST in adult cancer patients and their caregivers.[55-**56**] This measure has been shown to have good test-retest reliability and to discriminate between individuals who received PSST and those who did not.[56] This is a performance-based measure of problem-solving skills outcome (the ability to apply problem-solving principles to actual situations) and goes beyond measures of problem-solving process, such as the SPSI-R, which assess the cognitive and behavioral variables that contribute to problem-solving ability. In response to hypothetical vignette situations, subjects are asked to demonstrate specific skills and abilities (e.g., problem recognition and definition, generation of alternatives, decision making). As a performance-based test, the vignettes measure is intended to minimize the demand characteristics associated with instruments such as the SPSI-R that may reflect a subject's learning of problem-solving language during PSST, but not necessarily the ability to apply these principles. Measures of both performance and process, used together, provide a powerful assessment of the overall construct of problem solving.

Using the PST-C model, at each assessment point (T1, T2, T3), subjects will be presented with two vignettes selected at random from the pool of vignettes and asked to respond to four critical questions: **(1).** "What is the problem? What about this situation makes it a problem?"; **(2).** "Think of as many different ways to solve this problem as you can. Think of as many ideas as you can."; **(3).** "Which solution do you think is the best one? Which idea would you carry out to solve the problem?"; and **(4).** "For the solution you choose, what are some of the positive and negative consequences, that is good things and bad things, that might occur if you carried it out?" Responses are scored on 0-5 point Likert scales reflecting response quality, defined by operational criteria for relevancy, effectiveness, and accuracy. Detailed instruction for administration of the PST-C and scoring of responses appears in its manual).

Mood State

Depression will be measured using the Beck Depression Inventory (BDI).[57] This 21-item self-report measure assesses the cognitive, affective, and behavioral components of depressive symptoms. It is widely used for both clinical and research purposes. Internal consistency of the BDI ranges from .73 to .92, with good test-retest reliabilities cited in the test manual. The BDI has been used in a number of studies assessing the relationship between problem-solving ability and depression and is included, in addition to the Profile of Mood States scale, to investigate the replicability of previous findings.

In addition to depression, other aspects of negative affectivity will be measured using the Profile of Mood States (POMS) Scale.[58] This self-report instrument, which consists of 65, five-point objective rating scales about feelings over the previous week, measures six moods or affective states (tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment). Internal consistency, test-retest reliability, and validity are acceptable. POMS is easily administered, can be completed in five minutes, requires a 7th grade reading ability, and can be hand scored. It is a sensitive indicator of change. The total mood state score will be used for initial analyses regarding mood state.

Post-traumatic Stress

The construct of perceived post-traumatic stress as a component of negative affectivity will be measured using the Impact of Event Scale-Revised (IES-R).[59] This 22-item self-report measure includes three subscales (intrusion, avoidance, and hyperarousal) that assess posttraumatic stress symptoms (PTSSx) during the past week experienced in response to a specific event. It has been used widely to measure PTSSx associated with significant events such as diagnosis with cancer. Internal consistency reliabilities of the intrusion, avoidance, and hyperarousal subscales are .91, .84, and .90, respectively.

Resource Utilization and Satisfaction

This listing of typical resources is adapted from the National Health and Nutrition Examination Survey (NHANES) administered periodically to a representative national sample. In addition to questions regarding perceived usefulness/satisfaction with professional/community support resources that the mother has accessed we will also inventory perceived satisfaction with spouse/family/friends as a support network.

Credibility Measure: Expectancy Scales

At the end of sessions 1 and 4, each subject will complete a 3-item, 9 –point credibility scale and a 0-100% scale of expectancy for improvement. The measures will be administered by the RA but not seen by the RA as they are sealed in an envelope and sent immediately to the data management center

Timetable for Administration of Assessment Measures

MEASURE	TIME 1 (pre)	TIME 2 (post)	TIME 3 (3 mos. post)
	T1	T2	T3
Demographic Survey	X		
Hispanic Stress Inventory *	X		
Problem-Solving Skills Inventory	X	X	X
Vignette-based Assessment	X	X	X
Beck Depression Inventory	X	X	X
Profile of Mood States	X	X	X
Impact of Event Scale	X	X	X
Resource Utilization/Satisfaction	X	X	X
Process Evaluation (Maternal Feedback) Survey		X	

* Spanish language learners and controls only

Reasons for Early Cessation of Intervention

Medical crisis of the child as determined by his/her oncologist is a potential reason to withdraw from the study. The participant can choose to continue if she perceives the support derived from participation to outweigh the burden of participation.

Objectives and entire statistical section

Specific Aim 1: To measure more directly the efficacy of PSST, independent of social support, in reducing negative affectivity, we will develop a standardized social support

intervention consisting of eight 1-hour sessions to serve as a time and attention control condition (TACC).

Hypothesis: Mothers randomized to receive PSST will demonstrate higher levels of problem-solving skills and greater reductions in negative affectivity than mothers who receive the TACC.

Specific Aim 2: To develop, field test, and evaluate a hand-held supplement to PSST that functions as a readily available teaching aid and reinforcer of good problem-solving technique, we will develop an engaging, user-friendly program for a personal digital assistant (PDA) device that will provide information and positive reinforcement.

Hypothesis: Mothers receiving PSST + *PDA* will demonstrate a greater decrease in negative affectivity than mothers receiving PSST alone or TACC.

Specific Aim 3A: To measure a mother's knowledge and use of PSST in real-life everyday situations, we will develop an independent vignette-based measure of the application of PSST strategies to solve problems commonly encountered in the management of childhood cancer and compare findings from this measure with changes in scores on the Social Problem-Solving Inventory (SPSI), a standardized paper-and-pencil measure.

Hypothesis: Usage of PSST strategies as assessed by responses to vignettes of real-world situations will be greater among mothers receiving PSST than among mothers in the TACC and will be related to changes in SPSI scores.

Specific Aim 3B: To measure a mother's usage of PSST in vivo, we will develop a tracking tool that can be loaded satisfactorily into a personal digital assistant (PDA) device to periodically monitor the mother's actual application of PSST in real-life situations.

Hypothesis: Scores on the SPSI and the vignettes will correlate with problem-solving activity recorded by the tracking tool.

Specific Aim 4: To assess the efficacy of PSST as a problem management strategy, we will measure mothers' use of and satisfaction with other resources within the family and community, and from health, mental health, and social service professionals.

Hypothesis: Mothers receiving PSST will express greater satisfaction with the assistance given to them by the resources they access than mothers who do not receive PSST.

Statistical Considerations

Randomization

The randomization assignments will be balanced within site and language using as an undisclosed block size within the strata (see above).

Data Analysis

Although the proposed trial will provide a wealth of data for analysis, to guide future therapy more effectively it is important to identify a primary analysis *a priori*. The primary analysis will be performed on an "intent-to-treat" basis; i.e., once a subject is randomized, data on that subject will be analyzed according to their assignment, regardless of whether or not the subject actually completes the intervention. Every effort will be made to reduce attrition and to obtain post-treatment data on subjects even if they do not complete treatment. Steps will be employed to avoid the problem of missing data, including providing careful instructions to subjects, offering assistance throughout data collection, and making follow-up calls as necessary to obtain complete responses. (Note that in the just-completed study, only 6% of the follow-up assessments at T2 and T3 were missing.) If necessary, imputation strategies for handling missing data will be chosen based on the type, nature, and extent of the problem, and could range from replacing a single item on a scale with the mean of the subscale, dropping a subscale or measure, or multiple imputation for the primary endpoints.[69]

Aims #1, 2, and 4

General Considerations

Analyses will be performed using maximum likelihood estimation (MLE) for incomplete repeated measures.[46-47] This approach has several advantages: (1) All available data on eligible subjects can be included in the analysis even when there is missing data at follow-up; (2) It estimates the correlation between related measures and adjusts test statistics appropriately; (3) Time varying covariates can be incorporated into the model; and, (4) The assumptions about missing data are relaxed from Missing Completely at Random (MCAR) to Missing at Random (MAR).[70] The primary endpoint will be the estimated change from T1 to T2 in problem- solving skills including the vignette measures, negative affect and IES-R in the combined English and Spanish speaking mothers. The change from T1 to T3 will be considered a secondary endpoint. Because the outcomes of interest are correlated over time ($p>.5$), the power is increased relative to cross-sectional comparisons. The primary analysis will not explicitly consider the pre-stratification variables unless there is a strong imbalance across the two groups, but the effect of these variables on outcome will be investigated as secondary analyses.

Construct Development/Reduction of Multiple Endpoints

Each of our primary outcomes is assessed using multiple measures. Our initial plan for analysis of these data will be to use a systematic approach to reduce the multiple measures of negative affect (BDI, POMS, IES) and problem-solving skills (SPSI and the vignettes) to two construct measures. The construct building approach[71] is advantageous because it allows us to perform fewer analyses, minimizing Type I error; increases the power to detect differences in related measures which are all in the same direction, and produces a more robust indicator of the respective latent variable. The procedure will be to examine the internal consistency of each overt indictor (subscales or tests) using Cronbach's alpha and item- total correlations. The *a priori* requirements are Cronbach's alpha > .60 and item-total correlations >.20. A confirmatory factor analysis will be completed on the set of scales making up each of the two constructs, splitting the sample randomly into two groups. Assuming that the results of this step are satisfactory, constructs will be calculated by summing the standardized scores, where the baseline mean and variance estimates will be used to standardize the scores. Previous work with this strategy by Noll, a member of our collaborative group, has been successful for reduction of multiple measures of family functioning from multiple sources[72] and for the reduction of pediatric neuropsychological data.[73] If this approach does not result in single indicators of our primary constructs, we will use the data from multiple measures to assess the impact of our intervention.

Mediational Model

One approach for testing for mediation by a construct measured by a single variable is the regression approach outlined by.[74-75] Specifically, four conditions must be met: (1) the predictor (PSST intervention) must be significantly associated with the mediator (Problem-Solving Skills); (2) the predictor must be significantly associated with the outcome (negative affect); (3) the mediator must be significantly associated with the outcome; and (4) the predictor explains less of the variation in the outcome after controlling for the variation explained by the mediator. [Note, if the second condition is not satisfied, the PSST has an indirect effect on the outcome.]

Aim #3: Vignette Measure Development

Development Pilot

Six subjects per site or 36 total subjects will complete 4 of the 12 proposed vignettes. Thus, 12 subjects will complete each of the vignettes. The pool of 12 vignettes will be reduced to a pool of 6 vignettes by excluding those in which the % agreement among the raters is less than 80%, with evidence of floor or ceiling effects, or limited range (variance<4 for a 0-20 point scale).

Main Study

Because of a concern about a strong learning effect over time with respect to the vignettes, different vignettes will be presented to each subject at each of the three assessments. The order of the vignettes will be determined at the time of randomization and assigned so that the vignettes are balanced over time and intervention group. During the course of the study, 20% of the vignettes will be randomly selected and scored by two investigators (Dr. Dolgin or Dr. Phipps, and Dr. Sahler) to monitor the level of agreement among the raters.

Assessment of Treatment Effect

Analysis of the scores from the Problem-Solving Vignettes will use a mixed effects model for the incomplete (unbalanced) design. This modified model is necessary because of the random assignment of different vignettes at each of the three assessments. The proposed model is: $Y_{hijk} = \mu_{hj} + \alpha_k + \gamma_i + \varepsilon_{hijk}$, where *h* indicates the intervention group, *i* indicates the subject, *j* indicates time, and *k* indicates the vignette. μ_{hj} are the fixed effect parameters of interest that will be used to test the primary hypotheses. α_k will model any differences in the inherent *difficulty* of the vignette, $\sum \alpha_k = 0$. γ_i will be a random effect modeling variation among subjects and the residual errors will be used to model the within-subject correlation across time and the six vignettes. Estimates of α_k, if significantly different from 0, will be used to calculate standardized scores that will subsequently be used to examine the correlations between the Problem-Solving Vignette scores and the SPSI-R.

We will also assess internal reliability, concurrent validity (correlation with the SPSI-R) and discriminate validity (differences associated with PSST vs. TACC).

PDA Statistical Analyses

As noted above, a set of records will be created for each activation of the PDA application; data captured will be a log of all PDA usage including the following:

- Date and time of activation of PDA application

- Screens/panels displayed and menu choices selected
- Responses to all questions presented including date and time stamps
- Voice capture of any responses where voice input is allowed

Data will include identification of initial problem input as well as updates of previous problems. Updates will include identification of new strategies, selection of alternative strategies, and evaluation of current strategies.

Recorded data will be summarized weekly to generate summary measures such as the number of times (or days) the PDA was activated, number of times (or days) specific screens/panels were selected, number of new problems, resolution. These weekly summary measures will be examined for trends over time in usage, using longitudinal models. Depending on the distributions of the scores, we may use longitudinal models for normally distributed outcomes (possibly after log or square root transformations) or Poisson regression for repeated measures (GEEs or quasi-likelihood methods). For these primary analyses, we will not attempt to code open-ended responses (including voice capture). However, these data will be available for *post hoc* analyses if requested.

Additional Analyses

Distributional characteristics of the data will be examined. Data transformation procedures will be used if non-normal distributions are found. Although subjects will be randomly assigned to treatment conditions, we will examine whether group differences in demographics or medical status exist at baseline using adjustments for analysis of multiple endpoints.[76] Exploratory analyses will be conducted to identify demographic characteristics that are associated with decreased problem-solving skills, increased negative affect and increased stress (IES-R) in mothers at T1. Other exploratory analyses will include models that explore the moderating effects of demographic characteristics such a maternal education in the entire sample and immigration stress within the Hispanic subjects. In each analysis, procedures will be used to minimize the Type I error rate. Strategies include specifying a minimum correlation (R^2>5%, rho>.22) for 'clinical significance' and requiring statistical significance of the overall model prior to examining statistical significance of individual explanatory variables. Additional exploratory analyses include differences in the effectiveness of the intervention delivered in English versus Spanish.

Statistical Power

General Considerations

We estimated the sample size necessary based on our experience in the previous trial. Estimates of the effect of PSST are obtained from the study of 429 mothers with the intervention delivered in English or Spanish (described in Section C. Preliminary Studies) using the same method of analysis as proposed for the current study. Moderate effects[1] (0.4 S.D.) were observed for the BDI and IES-R and smaller effects (0.2-0.3 S.D.) for the POMS and the problem-solving skills when compared to a no intervention control. With the TACC intervention we would expect some effect on the measures of negative affect, but not on the measures of problem-solving skills; thus the expected effect sizes for the PSST versus TACC are likely to be in the range of 0.2-0.3 S.D. With the addition of the PDA to the PSST, we expect a small effect (0.2-0.3 S.D.) relative to the PSST and a moderated effect (0.4-0.5) relative to the TACC in problem-solving skills. The incremental effect on negative affectivity is likely to be in the lower end of the range. Correlations between the T1 and T2 assessments ranged from 0.5 to 0.7.

Aims 1 and 2

We will enroll 250 mothers each on each arm and conservatively expect a 10% loss to follow-up; thus, at least 225 subjects with T2 and T3 assessments will be available. The power calculations (two-group comparisons, two-sided tests, alpha=0.05) are based on the following approximation: $Z_{1-\beta} = \left(\delta / \sqrt{2\sigma^2(1-\rho)\left(n_1^{-1} + n_2^{-1}\right)}\right) - Z_{1-\alpha/2}$ where n1 and n2 are the number of subjects with follow-up assessments. This formula takes into account the correlation among the repeated measures. Specifically, if the treatment comparisons are based on the change in the outcome (Y_{it}) from T1 to T2, the variance of the change in the outcome from T1 to T2 (Var [Y_{i2}-Y_{i1}]) is $2\sigma^2(1-\rho)$ where σ^2 is the variance of the outcome (Y_{it}) and ρ is correlation between Y_{i1} and Y_{i2}. Thus, the variance of the difference between the mean changes for two groups is $2\sigma^2(1-\rho)\left(n_1^{-1} + n_2^{-1}\right)$.

Power to detect differences in change from T1 to T2 or T3

(Aims 1 and 2)

N=250 randomized per group with 10% dropout at T2 or T3

1 Effect size is defined as the difference in the change from baseline between two arms divided by the standard deviation of the baseline measures.

	Effect size	Rho=0.5	Rho=0.6	Rho=0.7
TACC vs. PSST	0.20 S.D.	.56	.66	.78
	0.25 S.D.	.76	.84	.93
	0.30 S.D.	.89	.94	.98
PSST vs. PSST+PDA	0.20 S.D.	.56	.66	.78
	0.25 S.D.	.76	.84	.93
	0.30 S.D.	.89	.94	.98

MODIFICATION OF PROTOCOL REQUESTED 11/15/06

APPROVED 12/7/06

An amendment to the protocol was requested for two reasons: (1) We unexpectedly lost our technical support vendor late enough in the course of the project to make it impossible to undertake a software redesign. (2) Although we were able to proceed with the assistance of the technical expertise of one of the project research assistants and complete data collection on participants already enrolled, we began experiencing technical difficulties enrolling new participants into that arm that we could not remedy satisfactorily enough to proceed. We requested a change in study procedures/study design, a reduction in our accrual goal, and a change in the consent process. This amendment was approved through expedited review at each of the data collection sites, the data management center, and the umbrella (PI) institution.

The following are the changes made at that time:

(1) Deletion of Specific Aims 2 and 3B and their associated hypotheses.
(2) Deletion of the entire section in Methods regarding PSST + PDA.
(3) Reduction in recruitment goal from 750 to 600 participants (250 subjects each in Arms 1 (PSST) and 2 (TACC) and 100 subjects already recruited into Arm 3 (PSST + PDA).

The power calculation to detect the differences in change from T1 to T2 or T3 (Aims 1 and 2) were as follows given N=250 randomized/group with 10% dropout at T2 or T3.

	Effect Size	Rho=0.5	Rho=0.6	Rho=0.7
TACC vs. PSST	0.20 SD	.56	.66	.78
	0.25 SD	.76	.84	.93
	0.30 SD	.89	.94	.98

Please note: A qualitative analysis of our experience to date with mothers randomized to the PSST + PDA arm was performed and published.

Askins MA, Sahler OJZ, Sherman SA, Fairclough DL, Butler RW, Katz ER, Dolgin MJ, Varni JW, Noll RB. Report from a multi-institutional randomized clinical trial examining computer-assisted problem-solving skills training for English- and Spanish-speaking mothers of children with newly diagnosed cancer. *J Pediatr Psychol* 2009; 34:551-563.