Protocol for Comparative Efficacy of Self-directed & Therapist-assisted Telehealth Parent Training Intervention for Children With ASD

NCT02721381

Based on last approval by MSU IRB on 4/6/2020

Risk to Human Subjects

a. Human Subjects Involvement, Characteristics, and Design

A total sample of 90 children with ASD between the ages 18-96 months and their primary caregivers will be recruited for this study. This sample size was determined to be adequate for maintaining adequate power for the proposed statistical analyses, while allowing for some attrition.

Inclusion Criteria for Families: To be eligible for participation, 1) the child must receive a DSM-V-informed clinical diagnosis of Autism Spectrum Disorder, based on the *Autism Diagnostic Observation Schedule* (ADOS). The diagnosis may be provisional for children under age 3 (typically listed as "at risk for ASD"). Children with this classification will be included as well. (2) The child must fall between the ages of 18 - 96 months at enrollment into the study, which will allow for data collection during the period of early intervention and early childhood special education programming. (3) The parent must understand spoken English as the training materials are presented in English.

Exclusion Criteria for Families: (1) Children with ASD who have a history of significant brain injury or known neurological condition in addition to a diagnosis of ASD, significant sensory impairment or major medical problems. These children and their families may require very specific adaptations to the treatment and thus the results will not be representative of children with ASD. This will be determined through review of medical records, diagnostic reports and parent interview. Criteria and data sources for identifying participants are outlined below.

Assignment to Study Group: Participating children and their primary caregivers will be assigned to one of three groups. Participants will be stratified by age (18-35 months; >36 months) and developmental quotient (DQ<55; DQ ≥55) at project enrollment, prior to being randomized. After stratification, participants will be randomly assigned to the one of the three groups using random permuted blocks of 6. This approach has been shown to yield groups that are closely balanced with regard to size and relevant pre-treatment characteristics. All pre-treatment assessments will be collected prior to randomization to prevent bias during testing based on knowledge of future group placement.

b. Sources of Materials

The sources of data for this study will include: (1) direct assessment of child functioning using standardized assessments; (2) completion of standardized questionnaires by parents; (3) written survey completion by parents; and (4) videotaped coding of treatment processes. All data will be used exclusively for research purposes. All surveys and interviews will use codes rather than subject names. Only the PI and primary research team members will have access to subject identities. Procedures to minimize risk of loss of confidentiality are presented below.

Child Measures: Child diagnostic testing will be conducted at pre-treatment. We will also examine specific child characteristics (cognitive ability level, language level, autism severity) that are predicted to be related to the impact of the parent-implemented interventions. We will administer the Autism Diagnostic Observation Scale, 2nd Edition (ADOS-2) to the child at pre-treatment. The ADOS-2 is a standardized protocol for observation of social and communicative behavior associated with a diagnosis of ASD that has been shown to have high reliability and discriminant validity. Recent longitudinal studies have demonstrated that diagnostic stability for children under age 3 is best when using DSM-IV based clinical judgment in conjunction with results from standardized diagnostic instruments, such as the ADOS. As in previous studies, this is the approach that will be used in the present study in order to determine a specific DSM-V diagnosis for each child. The PI has established research reliability on the ADOS. She will train the clinical research staff on these methods (as needed) and supervise all assessments. Child cognitive ability will be assessed using the Mullen Scales of Early Learning at T1. Child intentional communication with the parent will be scored from a parent-child interaction in the home at pre-treatment and post-treatment using weighted frequency of intentional communication. Language outcomes will be assessed at pre-treatment and follow-up using the

Mullen Scales of Early Learning, a parent report measure (the MacArthur-Bates Communicative Development Inventory) and the Vineland Adaptive Behavior Scales.

Parent Measures: Parents will complete the Parenting Sense of Competence Scale at pre-treatment, post-treatment, and follow-up to assess parent self-efficacy. Using the videotapes of the parent-child interaction in the home at pre-, post-treatment, and follow-up, the research team will assess parent use of the intervention strategies. Parents will also be asked to provide demographic information and complete the Parent Expectancies for Therapy Scale, a measure of treatment expectancy, the Computer-Email-Web Fluency Scale, a measure of computer/internet fluency, at pre-treatment, and the Parenting Stress Index, a measure of parenting stress at pre-treatment. Parents will be asked to complete the Treatment Evaluation Inventory, measure of treatment acceptability, at the conclusion of treatment. Parents will complete the Additional Services Form to monitor the type and number of hours per week of all non-study treatments once per month throughout study participation.

c. Potential Risks

There are no known serious health or psychological risks related to participation in this study. Procedures to minimize risk of loss of confidentiality are presented in the following section. In addition, there are legal limits to the confidentiality of information obtained during the research study. All information obtained from participants will be held confidential unless there is serious threat of harm to a child or to self or others. These limitations will be addressed in the consent forms. Collection of data from participants will include standardized child assessment measures, standard parent questionnaires regarding their child's development and behavior, standard parent questionnaires about their well-being and satisfaction with treatment, and videotape recordings. Precautions will be applied to all collected data from these activities, which will be stored in a private, secure and confidential location at MSU. All participants will be made aware of how collected data will be handled.

Adequacy of Protection Against Risks

a. Recruitment and Informed Consent

Primary caregivers of children with ASD will be recruited to participate in this study. Recruitment will be conducted through our ongoing contacts in Intermediate School District preschool special education programs and with clinicians at a number of sites in Lower Michigan. If a child appears to be eligible for the study, the clinician at that site will introduce the study to the family and present them with a brochure about the research project. In addition, a description of the study will be placed on the P.I.'s website which the public can access. Families who wish to participate will contact the project manager directly. The project manager will contact families to further explain the study, answer questions and schedule the first assessment session. The project manager will schedule an initial interview with the parents. At the beginning of that interview, the consent documents will be reviewed and written consent will be obtained from the parent. No child assent will be obtained because all children are expected to have significant cognitive and language delays that would prevent them from giving informed assent. Potential participants will be informed about the purpose and nature of the study and their rights as a participant. Written consent will be secured prior to the initiation of study participation. Participants will be assured of the maintenance of confidentiality and informed of their right to refuse to provide any data. Participants will be assured that data will only be reported in aggregate form without any individual identifying information. Parents will be compensated with $25 for the pre-treatment, post-treatment, and follow-up assessment, totaling $75. Each assessment period will consist of three to four hours of testing, involving direct child assessment, parent interview, and on-line data collection which may be completed across one to two visits. Applications for informed consent will be submitted to MSU's Human Research Protections Program. The nature of the proposed Research Plan is very similar to approved

studies currently being conducted by the P.I. As required, all amendments will be submitted for approval before being implemented. Annual project renewals will be submitted as required.

b. Protection Against Risks

1. Protection of Confidentiality: The current research proposes to collect both (a) personally identifying data (e.g., name, birth date, ethnicity, etc.) and (b) research data (e.g., interviews, diagnostic data, clinical assessment data, etc.). When connected only to a numeric identifier, the majority of the research data does not contain information that could identify a participant. When possible, standard protocols containing a numeric research identifier will be employed to separate personally identifying information from the research data. Video files will be coded with only the unique numeric identifier. The PI has had substantial experience ensuring the safety and confidentiality of video data. Personally identifying information will be stored in a single database that is located in the PI's lab. This database will be encrypted and have an access password that is only known to the PI and appropriate research members. Research data collected will be coded with a participant's unique identifier, or number and personally identifying data will not appear on any research data. All individuals working on the study will sign confidentiality agreements to never disclose any individual information regarding any aspect of the study. All data will only be reported in aggregate form without any identifying information.

2. Legal Limits of Confidentiality: There are legal limits to the confidentiality of information obtained in the data collection process. As a Licensed Psychologist, Dr. Ingersoll is a mandated reporter of child maltreatment risk. Specifically, if direct evidence of child maltreatment is reported in a research interview and/or observed in one of the videotaped parent training sessions, the researcher will communicate any such concerns to the PI and it may be reported to Child Protective Services. The PI will evaluate any possible reportable content or event and will make the report, if she deems there to be significant risk to a child's safety and/or health. Similarly if there is direct evidence of imminent suicide, partner violence, or homicide risk expressed by a parent in a research interview or during training phone calls, researchers will be trained to document any concerns related to safety risk and communicate these immediately to Dr. Ingersoll who will be on-call at all times. She will evaluate any potentially reportable content or event; consult with other experts at MSU, contact authorities as warranted, and make immediate follow-up calls to respondents who are acutely distressed. Given the characteristics of the subject population, the prevalence of child maltreatment and other concerns that require breach of confidentiality (e.g., suicidal risk) is not anticipated to be extremely high, but awareness of these issues will be maintained. Participants will be informed of these limits of confidentiality in the consent form. Any adverse events will be reported to the MSU Human Research Protections Program and the assigned Program Officer at the relevant NIH institute within one week of the occurrence, and summarized in the annual progress reports.

3. Other Risks: While not an adverse event, general discomfort may occur as participants are asked to discuss sensitive information. Efforts will be made to minimize potential discomfort associated with participating in any portion of this research. Consent forms will inform parents that they may discontinue their child's participation at any point in time. To minimize any potential discomfort or inconvenience associated with the research interviews and child assessments, such interviews and assessments will be scheduled at the participants' convenience in the family home. The intervention that will be used with the participants with autism is based on well-established principles of Applied Behavior Analysis and developmental psychology that have been used with autistic individuals for many years without resulting in any physical or emotional harm. Due to the behavioral difficulties exhibited by the target population, there is a potential risk of subjects becoming frustrated or bored during the training procedure or child assessments. Empirically documented behavioral management techniques will be used to address any tantrum behavior in the child participants. These techniques will include redirection

(i.e., trying to get the child interested in a positive behavior such as playing with a new toy when exhibiting negative behavior) and positive reinforcement for positive behavior (e.g., praise, access to desired materials). In some cases, extinction (i.e., ignoring the child's negative behavior) will be used if the two previous techniques are not effective. When using extinction, the parent will not ignore any self-injurious or dangerous behavior. If the child becomes too upset (unable to calm him or herself down within 10 minutes) or if the participant's parent becomes upset at his or her child's distress, parents will be encouraged to discontinue training.

Potential Benefits of the Proposed Research to the Subjects and Others

Parents will be provided with a report of their child's assessment results at pre-treatment and follow-up assessment. These reports will include the results of a comprehensive diagnostic evaluation. This report will only be shared with the parents, with our standard caveat that the purpose of the evaluation was as part of their participation in a research study and therefore should not necessarily be considered the equivalent of a clinical report. In our experience, parents usually find these reports to be quite helpful and many choose to share a copy with their child's service providers. Parents randomly assigned to the self-directed and therapist-assisted telehealth intervention groups will receive an internet-based parent training intervention that will be adapted from an evidence-based curriculum. Parents in the control group will be offered access to the self-directed telehealth intervention at completion of the study. There are no other direct anticipated benefits of participation in this study. There is, however, anticipated benefit of the knowledge gained from this study regarding parent-implemented interventions to improve outcomes for children with ASD and their families.

Importance of the Knowledge to be Gained

Knowledge gained from this research study will provide much needed information about ability to provide parent training for families with a child with ASD over the internet. Data available to date indicates great promise for parent training in terms of improving child outcomes and improving the quality of life for parents. Parent-delivered interventions can be implemented for relatively modest costs and provide services to a large number of families, in contrast to the high costs and limited availability of intensive child-directed services. While these parent-focused programs are not meant to replace intensive child-directed services for children with ASD, they appear to provide complimentary benefits and help to ameliorate the need for autism-specific services in areas where providers are in short supply. The provision of parent training over the internet has the potential to greatly increase the number of parents who can access these services, particularly in underserved areas where access to intervention providers is limited.

Statistical Analysis Plan

Overall Approach. The current study will use the Intention-to-Treat model (ITT) in the analysis of the primary aims. The ITT approach requires that all participants who are randomly assigned be compared on outcomes regardless of their adherence to treatment, reasons for withdrawal, or missing responses. Accordingly, we will include all participants in data analysis, follow up participants who withdraw from treatment, and impute missing data, as described below.

Missing Data. We will use the Expectation Maximization (EM) algorithm in SPSS to impute missing data for analyses that require complete data (e.g., Process Macro).

Preliminary analyses. To determine the comparability of groups on non-treatment variables after randomization, group differences will be examined for all T1 pre-treatment and descriptive variables. If significant group differences are detected for a given variable, and the variable of interest, then the variable will be used as a covariate in subsequent analyses as appropriate.

We will also examine age and DQ effects and identify whether treatment effects are moderated by either.

Aim 1: ***To examine the comparative efficacy of self-directed and therapist-assisted ImPACT Online on parent outcomes at post-treatment and the 3-month follow-up.*** To test our primary hypotheses for Aim 1, we will use multilevel modeling with restricted maximum likelihood estimation to examine the effect of group assignment on our primary and secondary parent outcomes. Time point (pre-treatment, post-treatment, follow-up) will be coded as a categorical variable. Change over time across groups will be estimated with the main effect of time, and between-group differences in change in outcomes will be estimated with the group by time interaction.

Aim 2: ***To examine the comparative efficacy of self-directed and therapist-assisted ImPACT Online on child outcomes at the 3-month follow-up.*** Three measures of verbal language will be collected at pre-treatment and follow-up. If child language measures are sufficiently correlated with each other (r>.50), we will create an equally weighted composite variable by z-scoring and summing the language measures. ANCOVA will be used to test for mean differences between the three conditions at follow-up. Pretest values will be included as covariates.

Aim 3: ***To examine whether pre-treatment parenting stress moderates the effects of ImPACT Online on parent fidelity and parent self-efficacy at post-treatment.*** Pre-treatment parenting stress will be included in the MLM models as a covariate. The pre-treatment parenting stress by time interaction will be used to determine whether pre-treatment parenting stress moderates change over time, irrespective of treatment group. The three-way interaction of pre-treatment parenting stress, group, and time will be used to examine whether the relationship between group assignment and change over time (i.e., group slopes) varied by pre-treatment parenting stress. A significant interaction will be followed up by simple slopes analyses.

Aim 4: ***To examine whether gains in parent fidelity (or parent self-efficacy) and child intentional communication at post-treatment mediate the effects of the ImPACT Online on child verbal language at the 3-month follow–up***. We will conduct two serial mediation analyses using the PROCESS macro in SPSS to examine whether gains in parent fidelity (Mediator 1) and child intentional communication (Mediator 2) at post-treatment mediate the effect of ImPACT Online in child outcomes at follow-up. A second serial mediation analysis will be conducted to examine whether gains in parent self-efficacy (Mediator 1) and child intentional communication (Mediator 2) at post-treatment mediate the effect of ImPACT Online in child outcomes at follow-up.

Aim 5 (exploratory): ***To identify predictors of parent adherence to ImPACT Online for the two treatment groups.*** This exploratory aim will be addressed using a multiple regression approach in which level of therapist support (self-directed versus therapist assisted) and three individual-level factors (computer and internet fluency, expectancies of treatment, and treatment acceptability) serve as primary predictors of parent adherence. We will also examine sociodemographic variables as predictors as well.

Power Analysis. A series of power analyses were conducted using Borm, Fransen, & Lemmens'[89] method for estimating sample size for analyses including a covariate. This approach takes into account the degree of association between the covariate and the outcome (r) by adjusting the required sample size required for an analysis without a covariate by $1 - r^2$ and then adding one extra participant per group. In our case, the covariate is the outcome variable as assessed at the pre-test. Analyses predicting parent fidelity (i.e., Aims 1 & 2) assumed a T1 to T2 correlation in fidelity of r = .35, and for self-efficacy, the T1 to T2 correlation was assumed to be r = .75. Across the aims involving parent fidelity we found that a sample size of 90 participants would provide 80% power to detect moderate to large effects of treatment condition (e.g., Cohen's f = .32). For parent self-efficacy a sample of 90 would provide 90%

power to detect moderately sized treatment effects (e.g., f = .25). For the child language variables we assumed a correlation between pretest and follow-up of approximately r = .65 for each of the three measures. Analyses predicting child language variables at follow-up controlling for pretest language scores (i.e., Aims 2 & 4) indicated that a sample size of 90 participants will have approximately 90% power to detect a moderate effect size (f = .25) for treatment condition.