A RANDOMIZED TRIAL OF PROJECT IMPACT, AN EVIDENCE-BASED INTERVENTION FOR INFANTS AND TODDLERS WITH AUTISM SPECTRUM DISORDER

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RESEARCH PROTOCOL

ABSTRACT

One in 59 children has ASD; approximately 40% are diagnosed before three years of age.[2] The Individuals with Disabilities Education Act (IDEA)[17] entitles these children to services that address their delays and prepare them for school. Evidence-based treatments for infants and toddlers with ASD include a therapist-implemented component and parent training, with the expectation that parents will continue the intervention between therapist visits. There is growing interest in the effects of parent-mediated intervention for young children with ASD,[18] driven by the belief that empowering parents to use intervention strategies within daily routines is more developmentally appropriate than intensive, therapist-led interventions.[11] High-quality, parent-mediated EI improves long-term outcomes for children with ASD across a range of developmental domains.[7,16,19] It also improves parental self-efficacy and treatment engagement.[7,20,21] Several efficacious parent-mediated interventions have been developed in research settings. Beyond the question of efficacy – the extent to which these interventions achieve outcomes under ideal circumstances – there has been a growing call to test their effectiveness – the extent to which they work under real-world circumstances.[9,10] Researchers have pointed to the 'voltage drop' that occurs when evidence-based interventions move from the lab to the community,[22] and the need to test whether they are successful when community clinicians use them.[23-25] The World Health Organization bemoans the lack of effectiveness trials, which inhibits its ability to strongly recommend parent training.[26] While Project ImPACT is designed for community implementation, it has not been subject to a rigorous effectiveness trial.

Services in publicly-funded EI often are limited to 1-to-3 hours a week of therapist contact. Little data are available on how many contact hours are necessary to change parent behavior, produce positive child outcomes, or the associated cost-benefit. One small, non-randomized study found that a low dose of Project ImPACT was enough to improve parent-reported outcomes relative to the comparison group, but the sample size, lack of randomization, use of highly-trained academic clinicians, and lack of a comparison group at another dose of Project ImPACT limits interpretation of these findings.[19] In addition to providing data on effectiveness, our study also will estimate cost-effectiveness. There is little evidence about cost-effectiveness, which is needed to support resource allocation decisions.[27] While several studies simulate data to suggest that the costs of early intervention are offset by long-term savings,[28-31] only two studies comprise a formal, rigorous cost-effectiveness evaluation.[32,33] None has examined the relative benefit of an intervention at different doses, a critically important question to our community partners. In Philadelphia, the infant and toddler early intervention program spends $10 million annually for services for children with ASD. In the US, these services typically are funded with public dollars. It is incumbent upon service systems to support interventions that produce meaningful outcomes and to avoid the use of public funding for interventions below or above an effective dose. With better information about effective dose of intervention, service systems can more effectively direct and allocate public dollars.

Our pilot study will address a number of pressing questions, including: Can community clinicians successfully coach parents of children with ASD in evidence-based practice to achieve positive outcomes for their children and themselves? What dose is necessary to achieve change?

And what is the cost effectiveness of implementing evidence-based interventions at different doses? This project has the potential to dramatically improve the services families of young children with ASD in Philadelphia receive, and significantly improve long-term outcomes. Successful completion of the proposed study would provide the EI system with the information needed to bring this type of intervention to scale across the entire system. Findings from this pilot trial would serve as the foundation for an application for federal funds to conduct a large-scale, system-wide study of Project ImPACT implemented in all Philadelphia agencies serving infants and toddlers with ASD.

RESEARCH PLAN

The proposed study is highly innovative. Foremost, the choice of intervention, the study questions and the study design all were developed in partnership with leaders from Philadelphia's infant and toddler early intervention system, which increases the ecological validity and utility of the findings, and the potential for the study to lead to lasting changes in Philadelphia's early intervention system.[34] Second, the study comprises a field trial of an intervention for young children with ASD using community (as opposed to university-based) clinicians to train parents in the intervention. This model of testing effectiveness is rare, with similar studies published mostly from data collected outside of the United States.[15] Third, our sample will be culturally and socio-economically diverse, a limitation of almost all prior autism intervention studies.[10] Fourth, we propose to test two doses of the same intervention. While determining the most effective dose of intervention is of critical importance to the field, there has been no head-to-head comparison in a randomized trial. Fifth, we propose to measure family as well as child outcomes, which rarely have been reported in intervention trials.[35]

Setting for all Research Activities

In Philadelphia, children ≤36 months of age with ASD are eligible for treatment through the infant and toddler early intervention program. Risk is determined using the Modified Checklist for Autism in Toddlers.[39] Thirteen agencies provide these services. They use an interdisciplinary treatment approach, have a treatment philosophy that supports parent-mediated intervention, and provide home-based services. The early intervention system projects that >800 children with autism ≤36 months of age will receive services next year. On average, children receive 3.4 hours/week of services, about one hour of which comprises "specialized instruction," which Project ImPACT will replace. Children will retain all other services. In specialized instruction, therapists: 1) design learning environments and activities that promote skill acquisition; 2) plan activities that address the outcomes on the individualized family service plan; 3) provide families with information, skills and support to enhance child skill development; and 4) work with the child and family to enhance the child's development. Specialized instructors typically are bachelors-prepared individuals with early child development training.

Aim 1: Compare outcomes in young children (social communication and development) and their parents (stress and self-efficacy) randomized to one of three groups: A) treatment as usual, B) Project ImPACT delivered at 1 hour/week and C) Project ImPACT delivered at 4 hours/week.

Overview

We will compare the outcomes of young children and their parents randomized to three groups: A) treatment as usual, B) 6 months of Project ImPACT at 1 hour/week and C) 6 months of Project ImPACT at 4 hours/week. Observations of regular early intervention sessions between families and clinicians will provide evidence of adherence to the Project ImPACT intervention. Observations of parent and child interactions as well as direct assessments with enrolled children over the course of 6 months, will give information on changes in social communication and parent responsiveness and self-efficacy.

Sample

Clinicians. We will recruit 3 clinicians from each of the 6 participating agencies (18 total). Agencies employ an average of 43 clinicians (range 21-64). Clinicians employed in these agencies have a Bachelor's or Master's degree in a related field, such as psychology, education, or speech pathology. Inclusion criteria are that the clinician: 1) has ≥ 5 children with ASD on their caseload; 2) agrees to participate in training and consultation if selected for one of the Project ImPACT arms; 3) identifies and obtains consent-to-contact forms for families on his or her caseload; and 4) completes the clinician study measures.

Children and their families. We will recruit 3 children per clinician (totaling 54 children, 54 parents). Inclusion criteria are that children: 1) be < 30 months of age (so that they can receive ≥ 6 months of intervention; 2) have a classification of autism or high autism risk as determined by the EI system; 3) be receiving early intervention services through the infant and toddler program and be participating in telehealth sessions if applicable; and 4) have a parent willing to complete the parent measures that are part of this study.

Setting

Assessments and fidelity observations will occur in the family's home, the usual provision of family-based early intervention services. The 2 day ImPACT training workshop will take place at a mutually desired upon location in Philadelphia convenient for clinicians to attend. Ongoing supervision and consultation will take place on video conferencing and phone calls.

Changes in response to COVID-19: The early intervention system is providing all direct service to families via tele-intervention. The research team will not visit families' home for any research activities until local and state authorities indicate that in-home intervention can be resumed. All research activities will be conducted remotely via tele-intervention, shared video recordings, and electronic surveys. Consistent with all services being delivered by the early intervention system, Project ImPACT and treatment as usual will be delivered via tele-intervention. The research team will join tele-intervention sessions for fidelity monitoring and coaching. Direct observation assessments will now be conducted via observations of self-recorded parent-child play interactions. Per these changes, families should have the ability and technology to participate in tele-health sessions with their EI provider in order to participate in the study.

Measures

Child Outcomes (all measures collected at baseline and 6 months):

Changes in Social Communication will be measured using the communication and social domains of the *Vineland Adaptive Behavior Scales–3rd Edition*[43] and the *Preschool Language Scales- 5th Edition* (PLS). The Vineland is a standardized parent report survey of adaptive functioning that has been normed on individuals ages birth to 90 years. It has excellent psychometric properties

and has been used in many studies of children with autism. Previous research has shown that Communication and Social Domain standard scores are sensitive to change in response to ImPACT.[19,44] The PLS is an interactive direct assessment of developmental language skills that can be given to children birth to seven years. Primary domains include auditory comprehension and expressive communication. It is designed to test a full range of communication skills across the developmental spectrum (including attention, play, gesture, and social communication). It has demonstrated strong reliability and validity across a diverse population, including clinical samples and children with ASD. We will use standard scores on auditory comprehension and expressive communication, as well as total standard scores, in the analyses. A research team member trained to reliability of administration will administer the PLS under the supervision of a licensed psychologist.

Changes in response to COVID-19: The Vineland will be administered to parents via a secure electronic survey link, instead of in person.

Children's Social Communication will be measured using the *Brief Observation of Social Communication Change (BOSCC*) scoring applied to the parent-child interaction videos, instead of the Preschool Language Scales. The BOSCC is an observational coding scheme designed to be sensitive to changes in social communication behavior, easily used by naïve, minimally trained examiners and coded relatively quickly. The BOSCC has strong interrater and test-retest reliability, sensitivity to change, and evidence of convergent and discriminative validity. The BOSCC scoring procedure will be used to measure child social communication behaviors during a parent-child play interaction. The BOSCC does not require direct contact with the parent or child to administer, so is an appropriate outcome measure to use in response to the COVID-19 pandemic. Parents will self- record a 10-minute play interaction between the parent and child using their phone, tablet, or any personal device and will share the recording with the research team via a secure Penn Medicine ShareFile link. ShareFile is a Citrix program that allows its users to share and receive large files securely.

Parent Outcomes (All measures will be completed at baseline, 3 months, and 6 months)

Parenting Self-Efficacy will be measured using the Early Intervention Parenting Self-Efficacy Scale (EIPSES),[45] a 16-item self-report measure that examines parents' beliefs about their ability to produce positive changes and promote optimal development in their child with a disability. It measures two dimensions of self-efficacy: Parent Outcome Expectations and Parent Competence. Parents rate items from 1 ("Strongly disagree") to 7 ("Strongly agree") with higher scores indicative of higher parenting self-efficacy. The EIPSES has strong psychometric properties and been used in a number of studies of families receiving Part C services.

Parent Quality of Life will be measured using the World Health Organization WOL Assessment-Brief (WHOQOL-BREF), a short version of the WHOQOL-100 scales. The 26-item questionnaire covers the four dimensions of QOL (physical, psychological, environmental, and social domains). The instrument measures the degree to which the respondent subjectively evaluates their satisfaction with different aspects of their life from a score ranging between 1 (very dissatisfied/very poor) and 5 (very satisfied/very good).

Changes in response to COVID-19: The EIPSES and WHOQOL-BREF will be administered electronically via a link unique to each participant sent via RedCap.

Parent Responsiveness will be measured using the Parenting Interactions with Children: Checklist of Observations Linked to Outcomes (PICCOLO),[46] a checklist of 29 observable, developmentally supportive parenting behaviors with children ages 10-47 months. The PICCOLO has four domains: Affection, Responsiveness, Encouragement, and Teaching. It is a strengths-based measure of parenting interactions that predicts children's early social, cognitive, and language development with solid psychometrics. A brief (10 minute) parent-child interaction will be video recorded (see below) at each time point; members of the research team blind to study arm or time point will score the checklist. Total scores on each domain are used to monitor change in parenting behaviors.

Parent Treatment Adherence will be assessed through a videotaped parent-child interaction at home. Parents will be asked to: 1) interact with their child for 10 minutes in the way they typically would during play; and 2) have a snack or meal with their child. Parent behavior will be scored for use of the intervention strategies using the Project ImPACT Intervention Fidelity Checklist.[1] Each of 6 strategies is scored on a scale of 1 ("Parent does not implement throughout session") to 5 ("Parent implements throughout session), and then averaged to form an overall fidelity rating for each routine. Ratings for the play and snack routines will be averaged to form an overall fidelity rating. Several studies have used the Project ImPACT fidelity checklist, which shows strong interrater reliability.[19,20,44] Trained observers blind to group assignment and time point will score it.

COVID-19 Changes: Parents will self-record a 10-minute play interaction and a snack routine with their child using their phone, tablet, or other personal device., instead of having a research team member record the session during a home visit. The same 10-minute play interaction will be used to code for changes in children's social communication as described above for the BOSCC, changes in parent responsiveness for the PICCOLO, and changes in parent treatment adherence (using the Project ImPACT Intervention Fidelity Checklist) for each time point. Parents will share the video with the research team using a secure Sharefile link.

Other Important Covariates will include 1) parents' socio-demographic characteristics. Parents will complete a form that includes demographics, family composition, education and financial resources using the relevant US Census Survey questions; and 2) clinician training and experience, which will be measured through a brief questionnaire that asks questions regarding degree, years in the field, experience with children with autism and experience with Project ImPACT components.

COVID-19 changes: The socio-demographic survey will be administered to parents via a unique secure electronic Redcap survey link.

Procedure

Clinician training

Dr. Ingersoll and the MSU research team will train community clinicians assigned to the Project ImPACT groups using a modified version of the published provider preparation protocol.[40] This 25-hour training will consist of a 6-hour, self-paced online tutorial, followed by a 2-day interactive workshop that covers the program's rationale and critical elements of the intervention techniques.

COVID-19 changes: The interactive workshop will be delivered to clinicians remotely via Zoom instead of in-person. The workshop will be delivered over 4 days, in 3.5 hour sessions, instead of 2 full days to accommodate the remote learning experience.

Following introductory training, clinicians in each agency will participate in bi-weekly group consultation meetings with Penn consultants (see below) via videoconferencing. During these 1-hour group meetings, clinicians will present their Project ImPACT cases to the other clinicians in their agency and receive feedback and problem solving from the Penn consultant. Each clinician also will receive a monthly consultation visit in the field. During these 1-hour sessions, the consultant will observe an intervention session, complete the coaching fidelity form, and provide feedback to the clinician on Project ImPACT implementation. Dr. Ingersoll's team has successfully used this remote consultation model to train clinicians to fidelity in Project ImPACT with high ratings of satisfaction, self-efficacy, and attendance from clinicians who participated in the training.[41]

To prepare Penn staff to consult in the field, Dr. Ingersoll and the MSU research team will train them to fidelity in Project ImPACT and its coaching model, and fidelity monitoring. This training will include the same introductory training described above, consultation meetings with MSU study staff to provide feedback on program implementation with a family with ASD via videoconferencing; and obtaining reliability on parent treatment adherence and coaching fidelity scoring for master session tapes. Once Penn staff have been trained to fidelity in coaching and reliability in fidelity monitoring, they will meet biweekly with MSU staff via video-conferencing for supervision as they provide monthly consultation sessions to community clinicians using Project ImPACT. MSU research staff also will conduct twice-a-month cross-site video-based fidelity checks to ensure that Penn staff is providing training and feedback to the clinicians implementing the program in a way that is consistent with the Project ImPACT model.

Clinician Fidelity will be measured using the Project ImPACT Coaching Fidelity Checklist.[1] Clinicians assigned to the two active treatment groups will self-monitor their coaching fidelity as part of the implementation procedure. We also will observe clinicians monthly to ensure accurate self-monitoring in the active treatment groups and to capture the extent to which clinicians in the treatment as usual group use any elements of ImPACT. Previous research indicates high interrater reliability between self and observer ratings on the coaching fidelity form (99% exact agreement);[42] thus we anticipate that self-ratings will provide an accurate measure of clinician behavior.

Cluster Randomized Study Design

Six agencies will be blocked into groups of 3 based on agency size and location. Within each group of three, each agency will be randomized to one of three conditions: 1) treatment as usual; 2) ImPACT at a dose of 1 hour/week over 6 months; and 3) ImPACT at 4 hours/week over 6 months.

Statistical Analysis for Aim 1

Outcomes will be analyzed as continuous variables at the child or parent level across time. Initially all outcomes will be described using summary statistics (means, medians, and estimates of variance). The longitudinal nested random effects linear models will be used for each outcome; the models will consist of three levels of random effects to adjust for individual child/parent, agency and clinician variability. For each measure, the analysis dataset will contain one observation with each subject's outcome measure at baseline and follow-up. The dependent variable in each model will be the measure of outcome at each time point. The independent variables will include a categorical variable for time period (baseline, 3 months, or 6 months), group (ImPACT_1hr/wk, ImPACT_4hr/wk or comparison), and their interaction. The magnitude and statistical significance of the beta coefficient for the interaction will provide an intent-to-treat assessment of the extent to which the intervention group improved relative to the comparison

group. Because agencies are randomly assigned, we expect clinicians and children in our intervention and comparison groups to be similar across baseline characteristics; however, if we find between-group differences we will control for them in our regression models.

Aim 2: Examine the cost effectiveness of Project ImPACT at different doses.

Overview

The purpose of the cost evaluation is to determine both the cost of implementing Project ImPACT in Philadelphia, and the cost associated with any additional benefit of one treatment arm over the other. Both questions are of great interest to our community partners and system administrators in general. Our cost-effectiveness analysis will take two perspectives: 1) a service perspective, which is of particular interest to policy makers and includes hospital, community and school-based health, social and education services; and 2) a societal perspective to capture the full economic implications, which also include parental out-of-pocket costs (insurance copayments, unreimbursed therapies and materials etc.), child care and schooling costs, productivity losses (time off work due to child's condition), and unpaid care.

Measures

Data on service and other resource use will be collected through parent report. To measure resources related to intervention implementation, we will document intervention implementation activities of agency partners, trainers/consultants, and experts from the investigative team in order to estimate total effort involved in implementation. Costs for the Project ImPACT groups will include: 1) initial training time of the agency clinicians; 2) subsequent consultation and coaching time provided to the clinicians; 3) clinician implementation of Project ImPACT with eligible children; and 4) consultant time necessary to maintain relationships with participating agencies/clinicians and support ongoing implementation of Project ImPACT. For each component, we will calculate two main types of costs: cost of physical materials used for training and interventions and costs associated with time spent for training, supervision, and intervention implementation. In addition, costs for initial training for the agency partners and trainers/consultants will be differentiated from the ongoing costs of implementation to provide separate estimates of costs for start-up in each agency and costs for ongoing implementation (with previously trained agency clinicians and trainers/consultants). Intervention and training/consultation times will be derived from the total Project ImPACT sessions delivered to each family each week and session logs completed by interventionists, trainers/consultants, and experts throughout the trial). To derive costs, we will use the resource costing method, which involves determining a price weight for each resource unit consumed where the price weight reflects the real opportunity cost of the service.[47] This price weight is then multiplied by the number of units at that price and then summed over all services. We will estimate the costs of clinician, trainer, and expert supervisor time using average salary and benefits for those in job categories matching the staff providing these services. We will cost materials using acquisition costs. We will determine unit costs for Project ImPACT services from a modified version of the Drug Abuse Treatment Cost Analysis Program (DATCAP).[48,49] This instrument is administered once and is used to derive price weights. This information includes salaries of personnel delivering services and other variable costs along with facility costs and other fixed costs associated with the intervention. The cost per hour will include provider costs and overheads (capital, administrative managerial) and travel costs. We will obtain other unit costs from published resources, national surveys, and government departments. We will calculate productivity losses using the human

capital approach, which involves multiplying time off work by the parent's wage rate.[50] We will calculate informal care costs using the market price approach that applies the price that would be paid if the care were provided by a formal care giver.[51] Finally, we will calculate total costs for each agency and then averaged across centers within each study arm to determine average costs per study condition.

Data Analysis

The outcomes of different study arms will be combined with their respective costs to provide a measure of relative cost-effectiveness that can be compared to other interventions employing the same measure of outcome. The effects will be improvements in child and parent outcomes. Using the estimated mean cost and mean effect per patient by intervention group, we will construct an incremental cost-effectiveness ratio for each outcome for which Project ImPACT shows a significant effect. Incremental cost-effectiveness will be computed as the ratio of the difference in mean costs (incremental cost) to the difference in mean effects (incremental effect), and will represent the additional cost per additional improvement in child development and social communication scores and parent stress and self-efficacy scores, of one intervention arm compared to another. A joint distribution of incremental mean costs and effects for the intervention arms being compared will be generated using non-parametric bootstrapping.[52] We will use these data to explore the probability that each treatment is optimal choice, subject to a range of possible maximum values (ceiling ratio) that a decision maker might be willing to pay for an additional improvement in child or parent outcome score. Cost-effectiveness acceptability curves (CEAC) will be generated by plotting these probabilities for a range of possible values of ceiling ratios.[53,54] CEACs are a standard decision-making approach to dealing with the uncertainty around the estimates of expected costs and effects and uncertainty regarding the maximum CER a decision maker would consider acceptable.[54] We will examine baseline characteristics across intervention groups to determine whether randomization was successful in balancing observed baseline covariates. If there is unbalanced allocation in baseline characteristics, we will use net-benefit regression to estimate directly in a regression framework.

Statistical Power

We base our statistical power analysis upon Aim 1, our primary aim, which tests the effects of Project ImPACT on child and parent outcomes. Prior studies of Project ImPACT and related parent-mediated interventions indi-cate a large effect on parent treatment adherence (.90-1.30), and a moderate effect on child outcomes (.34-.70).16,19,42 Meta-analytic reviews of studies of parent-implemented interventions for children with ASD report effects of .8 to 1.1.26 We used Power and Precision software, and assumed an alpha of 0.05, and that all tests are 2-tailed. We will have enrolled 3 clinicians in each agency and 3 children per clinician (18 subjects per inter-vention group). Due to statistical software limitations in addressing multiple levels of clustering in power estima-tion, we adopted two perspectives. First, we explored potential effect sizes (Cohen's d) with nesting of clinicians within agencies. Second, we estimated potential effect sizes with nesting of patients within clinicians. We as-sume an intra-class correlation of 0.05. In the first case, we calculate that we will have power of 80% to detect a moderate intervention effect of d=0.66. In the second case, we calculate that we will have power of 80% to de-tect a moderate intervention effect of d=0.53.

PROTECTION OF HUMAN SUBJECTS

Research will not begin until the Institutional Review Boards of the University of Pennsylvania and the City of Philadelphia approve the proposed study.

Characteristics of Population

We anticipate the sample of parent-child dyads will be 45% African American, 26% Latino, 18% Caucasian, 6% Asian, 2% American Indian/Native American, and 3% multi-racial. Children will be less than 3 years of age, and will either have a diagnosis of autism spectrum disorder or be identified as at-risk for autism by the early intervention system, as children under three years of age do not need a formal diagnosis to receive autism-specific treatment. We anticipate that 75% of the children will be male based on the sex distribution of autism. Participants will be excluded if they do not speak English. This is due to the procedures of the project, which include coding of videos of early intervention sessions. The team currently does not have capacity to code videos that are not in English. Participants will not be excluded based on their gender or past experience.

Data to be collected from Human Subjects

Data will take the form of demographic questionnaires, questionnaires, direct observations, direct assessments and video recordings. Data will be obtained directly from participants in the proposed research project.

Field Observations: We will collect direct observation ratings of provider's coaching fidelity using *the Project ImPACT Coaching Fidelity Checklist*. We will also collect direct observations of parent/child interactions that will inform the parent's adherence to treatment using the *Project ImPACT Intervention Fidelity Checklist* and parent responsiveness using the *Parenting Interactions with Children: Checklist of Observations Linked to Outcomes (PICCOLO).*

Demographic Questionnaires: We will collect sociodemographic information for each participant including information related to race/ethnicity, socioeconomic status, and education level.

Questionnaires: We will collect questionnaires from parents examining their self-efficacy using the Early Intervention Parenting Self-Efficacy Scale (EIPSES), and on their quality of life using the World Health Organization QOL Assessment-Brief (WHOQOL-BREF).We will measure changes in social communication by administering the *Vineland Adaptive Behavior Scales–3rd Edition* with parents. We'll also ask parents to fill out the Project ImPACT Parent Satisfaction Survey to evaluate how satisfied they were with the program overall.

Assessments: We will use the BOSCC to assess children's social communication and play skills from self-recorded 10-minute parent-child play interactions.

COVID-19 changes: All surveys will be administered electronically using a unique secure Redcap survey link. All sessions will be delivered via tele-intervention, consistent with current practice guidelines in the county. Fidelity observations will be conducted via tele-intervention.

Service Use: We will gather data on service use by interviewing parents regarding the total and type of services their child receives. We will interview parents about service use at screening and update during the 3-month and 6-month timepoints using the Service Utilization Survey that the research team will fill out.

COVID-19 changes: Interviews regarding service use will be conducted via telephone/video calls instead of in-person.

Recruitment and Informed Consent

Recruitment

Clinicians

Clinician recruitment will occur through the directors of the participating agencies. Recruitment and retention strategies are based on our prior community trials in which we recruited 80-95% of eligible practitioners and experienced 5-7% attrition. Each agency director will distribute flyers to clinicians in their employ to describe the project and invite them to participate. Agency leaders also will describe the study at staff meetings. Team members will attend professional development and informational meetings throughout the winter and spring of 2020 to answer clinicians' questions, address their concerns, and garner support. Study training activities will fulfill Pennsylvania's annual training requirements for early intervention clinicians, which is a considerable economic benefit to the clinician and the agency. Each clinician will also receive up to $150 for completing the Project ImPACT training workshop. There will be a local number and e-mail address for staff to contact with any study-related questions.

COVID-19 changes: Clinicians will be paid $150 for completing the training. The training is now being delivered across 4- 3.5 hour sessions, instead of 2 full days. Clinicians are not able to work during the training and are not paid by the county for the training time, as it is an external training. The compensation was increased to account for the increased time commitment across extended days for the remote training and subsequent loss of wages.

Families

Children and their families will be recruited and retained through clinicians and service coordinators who interact with families during evaluations and individualized family service planning meetings, with a flyer and brief video describing the study. As clinicians are recruited, they will refer families on their caseloads who have not yet responded. Participating families who successfully complete the measures will receive $50 at each data collection point. There will be a local number for families to call with any questions related to the study protocol.

Consent Process

All primary data collection will be conducted based on informed parental or practitioner consent. All signed consent forms will be maintained in the case file along with all identifying information in a locked cabinet that is kept in a secure office. The consent form includes the following elements: Purpose, Selection, Procedures, Risks, Costs and Financial Risks, Alternatives, Benefits, Payments, Confidentiality, and Withdrawal.

Clinicians will be informed about the study via a letter from their agency director. The letter will describe the project and ask them to participate. Agency Directors will also describe the study and answer questions at staff meetings and distribute study flyers. Study team members will also attend professional development and informational meetings to address questions and concerns and garner interest and support. Clinicians who are interested will be able to reach out to the study team directly in order to start study procedures.

All six participating agencies will be randomized into three groups based on their agency size and location. Interested clinicians at each agency will be informed of the randomization group during the consent process and are free to decline participation at any time.

Children and families will be recruited and retained through their clinician who is participating in the study as well as service coordinators at participating agencies who interact with families on a regular basis. Clinicians will refer families on their caseload and provide them with a flyer and brief video describing the study. Families who are interested in participating will reach out to a member of the study team in order to have questions and concerns addressed and see if they are eligible to participate.

All participants will be required to sign a written consent form in order to participate. During this process, participants will have the opportunity to ask questions about these consent forms prior to giving written informed consent. This document includes a description of the entire study and expected roles and responsibilities of the practitioner, primary caregiver and child, risks and benefits to participants, and confidentiality procedures. The consent document will also clearly state that participation in the study is completely voluntary, and participants can drop out of the study without penalty at any time. Study staff will review this consent form at the first face-to-face contact. At this time, study staff will answer questions and obtain written consent from the participant. The consent forms explicitly outline the voluntary nature of participation in this research study. Easy channels of communication to study staff in the event that a participant wishes not to participate will be clearly outlined. Specifically, the contact information for the PI and study coordinator will be listed on the consent form, expectations for participation, compensation and further outlines of confidentiality practices specific to information collected. All consent documents follow the guidelines outlined by the Office of Human Subjects Protection of the National Institutes of Health, the University of Pennsylvania, the City of Philadelphia EI system, and ethical guidelines set forth by the state and federal governments. Documentation of subject consent will be stored in a locked file in the PI or designees locked office.

Note: Per protocol changes, participants who signed earlier versions of the consent form that did not contain allowances for using videos for education purposes (consultation meetings) will be reconsented.

<u>In response to COVID-19 informed consent will be obtained electronically.</u> First, an electronic enrollment packet will be e-mailed to individuals who have expressed interest in survey completion. The enrollment packet will include an electronic, informed consent form via the University of Pennsylvania's Qualtrics portal, and an informational flyer about the survey component of the study. The research team will provide detailed information about the study via phone, and participants will complete a screening eligibility survey. If they meet eligibility criteria as outlined in the research protocol, they will view the informed consent document. The consent document includes a description of the study and expected roles and responsibilities of the provider, risks and benefits to participants, and confidentiality procedures. The consent document will also clearly state that participation in the study is completely voluntary, and participants can drop out of the study without penalty at any time. Consent will be obtained through the Qualtrics electronic survey consent form

Subject Compensation

Participating providers and families will be compensated for time spent completing data collection steps.

Providers
Clinicians in the Treatment as usual group will receive $25 for completing self report fidelity measures after each video recorded observation of their early intervention session. We will observe 3 sessions per family and enroll up to 3 families per provider. They may receive up to $225 for completed self-report fidelity after observations (3 observations at $25 each x 3 families)

Clinicians enrolled in one of the ImPACT groups and attend the 2 day project ImPACT interactive workshop and complete the self-paced, online training course, will be compensated $ 150 for their time. They will also receive the same compensation schedule as clinicians in the Treatment as Usual group for the self report fidelity measures.

Families
Families will receive $50 at each data collection point. There will be three data collection points for a total of up to $150.

Data Sharing

If providers believe that their performance in the study may be evaluated by their agency or the EI system they may become anxious and thus make them unlikely to participate in the study. Videotaping provides concrete examples of coaching techniques that enable efficient and accurate measurement of the strategies used during intervention sessions; however, there is potential that such videotaping will provide concrete examples of intervention techniques or other behavior that could negatively influence staff performance review if administrators or supervisors in the EI system were to view it. For this reason, there will be no disclosure of videotaped performance or self-reported information about provider fidelity, especially to these personnel. As a result, the research team will keep all identifiable and individual participant data confidential from all administrative personnel, including agency executive and clinical directors, and any other staff member of the Department of Behavioral Health and Intellectual Disabilities. Written notification of this procedure will be provided to all involved parties at the Philadelphia Department of Public Health. However, upon conclusion of data analysis, the research team will provide anonymous and aggregate results of the study to the Philadelphia Department of Public Health, the department of Intellectual and Disability Services within DPH, as well as any participating community agencies. Anonymous and aggregate results provided to community agencies will be aggregate data from all participants, not exclusively those from any single community agency. This procedure acts in the interest of participant confidentiality and job security.

Potential Risks to Subjects

Risk to children and parents.

Parent and child involvement in the proposed study involves direct observation measures of parents and their children in their homes and the parents' completion of measures about their children's behavior and their own self-efficacy. Additionally, all children will be assessed to gather information about their social-communication and language skills. The study provides training to parents and to the clinicians working with their children that otherwise would not be available. Parents' time commitment across all study arms is similar to usual practice. The study therefore involves minimal risk to children and their families. The risks include:

1) Respondent burden associated with the time and effort to complete the proposed battery;
    a. We estimate time burden to be an average of 1 hours for data collection from the child at baseline and at 6 months. Time burden for parents will average 85 minutes at baseline, 3 and 6 months. Relative to other studies that involve clinical assessment of children with ASD, this is a relatively small time commitment.
2) The possibility of breached confidentiality by disclosure of personal information;
3) The risk of distress caused by participating in the intervention;
    a. The proposed measures include a number of sensitive items related to children's clinical presentation and family characteristics. Evaluations of children may cause them fatigue or anxiety. Some questions asked of parents (such as those about income) may cause parents some discomfort. Risks involved with participating in the child assessments are expected to be minimal, given that process will be supervised by a trained clinical psychologist.
    b. Parents may feel anxious by observations or videotaping, especially if they believe that the research team is evaluating their performance. Videotaping provides concrete examples of teaching techniques that are vital to the measurements proposed in this research. However, there is potential that such videotaping will provide examples of behavior that the research team believes endanger the parent or child. For this reason, there will be no disclosure of observed or videotaped information to those outside of the research team unless there is a suspicion of child abuse or neglect. Parents will be informed during the consent process that all study personnel are mandated reporters. All staff are trained in mandated reporting and we have an approved reporting protocol for all of our community work. In cases of suspected abuse or neglect, the research staff member suspecting the abuse or neglect will contact one of the two licensed psychologists on the study. They will review the situation together and determine if it meets criteria for reporting.
4) The risk that the intervention may have some iatrogenic effect.
    a. There is a small chance that the proposed intervention may have negative consequences. The majority of evidence suggests that the components of the proposed intervention are the most efficacious in educating children with ASD; their effectiveness in this particular setting has not been tested, however.

Risk to clinicians

Clinician participation in the proposed study involves direct observation measures of their implementation of their practice. It also involves completing measures on their practice. The study therefore involves minimal risk to clinicians. Possible risks include:

1) Respondent burden associated with the time and effort to complete the proposed battery;
    a. We estimate that the time burden to clinicians for the proposed measures is 65 minutes at baseline, 3- and 6-month time points. Observations of clinician's practice will occur during their regularly scheduled home visits. Completing the fidelity checklist will take 5 minutes per visit.
2) Distress caused by the questionnaires, the interview or fidelity measures;
    a. Providers may be made anxious by videoing, especially if they believe that their performance in the study may be evaluated by their agency or the EI system. Videotaping provides concrete examples of coaching techniques that are vital to the measurements proposed in this research; however, there is potential that such videotaping will provide concrete examples of intervention techniques or other behavior that could negatively influence staff performance review if administrators or supervisors in the EI system were to view it. For this reason, there will be no disclosure of videotaped performance or self-reported information about provider fidelity, especially to these personnel. To help minimize this risk, we will provide EI administrative personnel, including agency executive and clinical directors, written notification that these measures are confidential and at no time and under no circumstances will be shared with EI personnel.
    b. Potentially more distressing are emotional responses to fidelity measures. The fidelity measures are designed to quantify EI providers' adherence to the intervention protocol. EI providers may feel as though their willingness or ability to treat children with ASD is being challenged. Specifically, documenting providers' performance may cause feelings of insecurity regarding effort or ability

3) The possibility of breached confidentiality by disclosure of personal information to agency or EI system personnel linking individual clinicians to their performance.

Protection against Risks

Interaction with research participants. To minimize distress associated with respondent burden and distress associated with the proposed measurement batteries, both parents and clinicians will be told at the beginning of each observation, or have stated at the beginning of each questionnaire that they may refuse to participate in any part of the study and skip any question at any time during the interview. We will accommodate parents' wishes with regards to the timing of the data collection and assessment, will break up the data collection into stages if requested, and will hire and train research staff to be sensitive to the well-being of children, parents and clinicians. Participants will be reminded that information will be kept confidential and will never be published in any manner that would identify them. Children's distress is most likely to arise from stress or fatigue associated with testing, frequent breaks will be offered along with snacks if desired. Tests

will be administered to children by trained professionals experienced in the procedures and sensitive to participants' clinical conditions. All participating families will be reminded that all clinical data will be collected for research purposes only. Families will be encouraged to contact their pediatrician, school evaluation center, or local developmental specialists if they desire further evaluation. A list of community referral resources will also be provided to all families.

Data Management and Access. To minimize risks associated with breaches of confidentiality, all data on study participants will remain confidential at all times. The exposure of the identity of study participants will be avoided wherever possible. An 11 digit identification number will be employed to encode the participant identity on study materials, including data collection forms. The Center for Mental Health at Penn, where data will be stored, has a 20-year history of conducting research using protected health information and linking it with other datasets. Center protocols for data management and protection have been developed and implemented for all datasets that include protected health information. The research team will handle the original media on which data are kept. Media will be labeled confidential, use only unique identification numbers and be kept in a locked filing cabinet. Penn's technology support services employ a number of security and privacy technologies and best practices in order to deliver services that provide "security in depth".

To ensure the privacy and confidentiality of data for this project we will only store and use the identifiable data at the following locations: 1) Password-protected PCs in locked offices at Penn. 2) A server at the University of Pennsylvania within the facilities managed room in the data center. A Senior LAN Consultant will upload the data onto the secure production servers. Videos will be sent from Penn to Dr. Ingersoll's lab at Michigan State University for coding. Videos will be sent via Penn Box, Penn's secure file sharing service. When viewing videos at MSU, staff will keep the video copy in Penn Box and not make copies to other media. Lastly, all output containing individual identifiable information is treated as confidential data. This information is never transferred electronically via email or other protocols. Any printed material containing individual identifiers is shredded.

Physical Security – Servers are hosted in dedicated virtual machines running on Dell SAN hardware in the Information Systems and computing facilities managed computer room. The hosting environment SAN and Host Bus Adapters are in a locked Dell rack housed in the Computer Room with restricted door card access to authorized personnel only. There is 24-hour camera surveillance.

Business Continuity – Server environments get redundant power from independent power feeds. In addition, each of the power sources is UPS protected. There is a Halon fire suppression system, with alarm points below the raised floor and in the ceiling. The virtual machines are hosted in VMWare ESX environments connected to a Dell SAN for shared storage. All virtual machines are stored on the SAN. To minimize downtime caused by hardware failure, the environment is configured for redundancy with multiple ESX hosts, multiple Host Bus Adapters, multiple SAN Switch ports, multiple storage processors, and RAID 5 storage. The server environments are replicated to a secondary site at 3650 Chestnut Street, which has equivalent physical security and also employs all of the security best practices outlined below.

Server Administration and Maintenance – The servers are administered by a team of four full-time professional IT staff. The team has over 50 years of combined experience configuring and

supporting Windows servers, and all of the staff attend technical training regularly to stay current in best practices for configuring and securing Windows and VMWare environments.

Server Security Best Practices – In keeping with SANS and Microsoft best practices, all software services and corresponding ports on the servers that are known to be substantial security risks and which are not used by CMH resources are disabled including telnet, and ftp. Security patches are applied promptly and there are standard processes in place for preventive maintenance and monitoring of the servers.

Hardware Firewalls - All servers reside behind a cluster of Juniper SSG520 firewalls. A Juniper SSG520 appliance configured in high availability mode acts as a secure gateway between PennNet/Internet (Untrusted Zone) and server resources behind the firewall. A custom firewall policy is developed for each resource hosted on each of the virtual machines. All policies are developed based on service port and PennNet only IP addresses.

VLAN - A Foundry Switch in the TSS managed rack is configured for 4 VLANs to support traffic segmentation behind the SSG520. LTS has access to each VLAN, giving us the ability to place each virtual machine in the appropriate VLAN for another layer of security.

SSL Encryption for Web Services - When hosting web servers we only support the use of HTTPS with an SSL certificate to minimize vulnerabilities and exploits common on the standard HTTP port. All port 80 traffic is re-directed to port 443.

Password Policy - A complex password policy, meeting Microsoft complex password requirements, is in effect in the CMHPSR domain. The password policy requires all CMHPSR domain users to change their domain password every 180 days.

Preparation of Staff for Data Collection

All study personnel will have Patient Oriented Research certification from the University of Pennsylvania. Clinical personnel meeting with families and providers will hold a Bachelor's, Master's or doctorate degree. The PI will oversee the additional training and ongoing review of interviewers. Clinical research staff who conduct assessments will be trained to reliability and supervised by the clinical psychologist on staff. The PI will also provide all research assistants with training regarding culturally sensitive practices, and maintaining professional boundaries while visiting families' homes. The research team will travel in pairs for home-based visits as a safety measure for both participants and research team members.

To prepare Penn staff to consult in the field, Dr. Ingersoll and the MSU research team will train them to fidelity in Project ImPACT and its coaching model, and fidelity monitoring. This training will include the same introductory training community clinicians will receive as described in Aim 1, consultation meetings with MSU study staff to provide feedback on program implementation with a family with ASD via videoconferencing; and obtaining reliability on parent treatment adherence and coaching fidelity scoring for master session tapes. Once Penn staff have been trained to fidelity in coaching and reliability in fidelity monitoring, they will meet biweekly with MSU staff via video-conferencing for supervision as they provide monthly consultation sessions to community clinicians using Project ImPACT. MSU research staff also will conduct twice-a-

month cross-site video-based fidelity checks to ensure that Penn staff is providing training and feedback to the clinicians implementing the program in a way that is consistent with the Project ImPACT model.

Adverse Events

All unexpected adverse events will be reported by study personnel to the DPH IRB, the Project Officer at IES, and the IRB at Penn via standard adverse event reporting procedures. All adverse reactions will be noted and discussed thoroughly with the PI, mentors, and IRB to determine proper reporting procedures on a case-by-case basis.

Potential Benefits of the Proposed Research to the Participants and Others

There are some benefits to family/child and clinician participants. Families in the treatment conditions will receive training in intervention techniques considered best practice for young children with ASD. In addition, clinicians in the two treatment conditions will receive considerable training and support throughout their participation that has the potential to benefit the children they treat. The potential exists for great benefits to child-serving systems at large. Potential risks are reasonable given the safeguards proposed and the valuable information to be yielded regarding interventions for children with ASD.

Data and Safety Monitoring Plan

Since this study constitutes a clinical trial, although we are not studying experimental drugs, the intervention is experimental with the risks described in the Human Subjects section. Therefore, it is appropriate to have a Data and Safety Monitoring Board (DSMB) to monitor the study with an attendant monitoring plan as outlined below. The role of the DSMB will be to ensure that no unexpected untoward consequences of the intervention occur, and if they do, to implement safeguards to decrease or eliminate future risks. Any adverse events will be provided to the DSMB in real time. These adverse events include, but are not limited to, self-injurious behavior or inappropriate or threatening behavior with parents, or clinicians or research staff. Less serious adverse events related to the intervention will be compiled and summarized for the DSMB at their scheduled meetings. All other severe adverse events will be monitored by the principal investigator, the study coordinator, and the assessment team and will be reported to the DSMB regardless of a priori expectation or investigator assessment of likelihood of the study being the cause of the adverse event. The DSMB also will have the power to request further data from the principal investigator based on any concerns raised in the ongoing investigation. At any time during the study, based on its findings, the DSMB can put the study on either temporary hold or stop the study entirely after notifying the principal investigator and the IRB. In the rare case in which they must do so, the DSMB will generate a formal report to the principal investigator, the sponsor, and the IRB. This report would then be modified for a lay reader, a version for past participants and current participants would be produced, and the letter would be sent to all past and current study participants. The DSMB will first meet at the beginning of the study to review its charge and activities. It will then meet quarterly to review non-serious and serious adverse event rates, as well as preliminary efficacy data. It also will meet on an ad hoc basis if the real-time serious adverse events warrant meeting, in their judgment. The format of the meeting will include a presentation of the summarized data by the Principal Investigator (Pellecchia) and the

biostatistician (Cidav). The absolute rates of adverse events as well as the rate compared between the intervention and control groups will be presented. The Board will be composed of two faculty at Penn who are not associated with this intervention but have familiarity with autism intervention, and a senior staff member from Philadelphia's early intervention program.