Can a novel telemedicine tool reduce disparities related to the identification of preschool children with autism?

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Background

With the rising prevalence of Autism Spectrum Disorder (ASD), accurate identification and meaningful engagement of children and families in evidence-based services represents a pressing public health and clinical care challenge. Considerable emphasis has been placed on strategies to boost early ASD diagnosis in toddlers. However, early identification is hindered in part by vast phenotypic heterogeneity, wherein subtle ASD symptoms may not be readily identified via screening, surveillance, or parent concerns during the toddler years. Specifically, children without significant language delays, cognitive delays, or externalizing behaviors may not be flagged as for ASD concerns until the preschool years or later. In addition, pervasive service system limits such as a lack of trained providers and significant wait times for evaluation can delay definitive diagnosis for years. Despite advances in screening and awareness, the average age of diagnosis in many locations in the US remains later than four years of age. This is especially true for children from traditionally underserved communities (e.g., families in poverty, rural communities, racial/ethnic minorities, linguistically diverse families), who are much less likely to be diagnosed at young ages. These delays contribute to substantial family stress and restrict access to ASD intervention services critical for optimal short-term and lifespan functioning.

Ideally, universal ASD screening in toddlerhood would identify most children at-risk for ASD and then facilitate prompt diagnostic evaluation by a multi-disciplinary team of specialists. In reality, such diagnostic teams, or individual experts, are not readily available in most areas of the U.S. The standard of care in many community pediatric settings is to perform developmental surveillance, screen for risk, and then refer children to tertiary diagnostic centers with lengthy waitlists; meanwhile, without diagnostic confirmation, children may receive low levels of non-specific intervention or preschool services, or fail to engage with intervention and school services at all. Data suggest that the wait for ASD evaluation services dramatically increases as children age, with extended waits (i.e. over a year) common in the preschool period. Delays in diagnosis may contribute to more pronounced impairments and challenges accessing services (i.e. diagnostic delay associated more limited private/school-based intervention, higher rates of psychotropic medication use). Unfortunately, even when an appointment becomes available, multi-stressed, rural, or traditionally underserved families may not be able to make it to a tertiary care center. Powerful recent work suggests that addressing care disparities and systemic structural racism within models of ASD identification will require novel identification tools and processes that 1) include the preschool age span and 2) specifically target underserved groups at risk for tremendous diagnostic delays. For example, a recent study investigating a large cohort of African-American children in the U.S. found an average 3-year delay between first parental developmental concern and ASD diagnosis; half of parents reported seeing multiple providers before receiving an ASD diagnosis, and 31% reporting a lack of available professionals as a major contribution to this delay.

Study Purpose and Description

Innovative telemedicine practices could address many existing traditional barriers to ASD identification. Telemedicine has the potential to put linguistically and culturally

competent clinical expert virtual providers directly into communities during a critical window in which many vulnerable families may approach, or re-approach, care systems about developmental concerns that become more prominent with age. In the current proposal, we will develop and evaluate the potential clinical and familial value of a telemedicine-based ASD assessment tool, the **TAP-Preschool** (**T**ELE-**A**SD-**P**EDS-**Preschool**), designed to overcome traditional barriers to diagnosis and service access in underserved preschool populations that may not be readily identified or engaged by early screening and intervention systems.

A growing body of literature supports the use of telemedicine-based approaches to ASD assessment and intervention. This includes remote activities to assess infant social communication skills in the first year of life, coaching parents through administration of gold standard diagnostic tests, and provider coding and analysis of interactions that are video-recorded by caregivers. Results reflect high levels of caregiver and provider satisfaction and satisfactory agreement with traditional in-person evaluations, illustrating both the promise and feasibility of tele-assessment. However, most existing approaches are limited by a focus on screening rather than diagnosis, protocols requiring specific materials, or asynchronous analysis of submitted videos, which require resources that preclude broader use. Moreover, in current form, these tools are not designed or intended to yield a quantitative formal assessment of core ASD symptoms to support diagnostic decision-making. Further, although providers are increasingly exploring telemedicine approaches to ASD assessment in the context of the COVID-19 pandemic, there is limited published work to date on the use of real-time, caregiver-led ASD assessment in home settings *with diverse populations*. Our own work has focused almost exclusively on toddlers in this regard. Ultimately, very few viable tools with validated psychometric properties are available for use in current models of telehealth assessment and care.

Study Aims

In **Specific Aim 1**, we will generate optimally performing models and key behavioral targets for tool development. We will do this by applying machine learning models and the principles of feature engineering to a phenotypically rich clinical research data set of preschoolers with ASD and other developmental concerns (N=914: 594 ASD and 320 Non-ASD).

In **Specific Aim 2,** we will engage in a rigorous adaptation and translation approach to optimize design of the *TAP-Preschool*. We will include leading ASD assessment experts, providers dedicated to caring for underserved populations, and parents of preschool children with ASD from underserved racial/ethnic and linguistic groups. We will lead these groups in a design process in order to yield a set of interactive and play-based, parent-coached tele-assessment activities designed to 1) elicit observations tied to key computational features, 2) be deployed within a 30-minute timeframe, 3) employ inexpensive materials found in most homes, and 4) use accessible assessment instructions for real-time coaching of parents.

We will recruit 30 parent/child dyads (children ages 36 to 72 months) with existing diagnoses of ASD (n = 20) or other developmental concerns (n = 10) from our clinical

research database. Each participant will have recent data available from comprehensive evaluation tools (ADOS-2, cognitive functioning, adaptive skills). Children with and without ASD are included to provide information about TAP-Preschool usage across diverse phenotypic profiles. The sample size of 30 is deemed adequate for gathering detection of feasibility/acceptability issues and key feedback regarding measure modification for further validation.

Inclusion/Exclusion Criteria: Aim 2
Inclusion
- English/Spanish Speaking families
- Children 36-72 months of age
- access to a device capable of supporting Zoom
- already has participated in a diagnostic evaluation

Exclusion
- severe sensorimotor impairments

Specific Aim 3: Initial deployment, formative evaluation, and refinement of the TAP-Preschool:

We will deploy the preliminary *TAP-Preschool* with a small sample (n = 30) to assess acceptability/feasibility, potential clinical value for remote observation, and challenges that warrant revision. We will then use this data to modify the *TAP-Preschool* and deploy the refined tool with a new sample of clinically referred children (n=120). We will evaluate its ability to facilitate accurate telemedicine supported diagnostic decision-making.

We will recruit a novel sample (n = 120) parent/child dyads (children 36 - 72 months of age) referred for evaluation of ASD or developmental delays. These children and a primary caregiver will participate in a home-based tele-assessment session and a subsequent blinded in-person evaluation. We will again include English/Spanish speaking families with access to a device that will support Zoom.

Inclusion/Exclusion Criteria: Aim 3
Inclusion
- English/Spanish Speaking families
- Children 36-72 months of age
- access to a device capable of supporting Zoom
- has not participated in a diagnostic evaluation

-Exclusion
- severe sensorimotor impairments

Study Procedures

Initial deployment, evaluation, and refinement of the TAP-Preschool:
Consenting families will be scheduled for a single tele-assessment session with a consented licensed psychologist ("remote clinician") from our clinical research center

(n=10). This clinician will coach parents through the TAP-Preschool procedures. Although families will receive standard, basic support regarding tele-assessment procedures, they will not receive extensive training on the TAP-P prior to the session in order to mimic real-world use. All remote clinicians will be experts in ASD with training on the original TAP and ADOS-2 research reliability. Each clinician will participate in 3 sessions (2 children with ASD, 1 other developmental concerns). Clinicians will be blinded to child diagnostic status. Participating telemedicine clinicians in this aim will not be aware of the ratio (2:1 ASD vs. other DD) or recruitment status prior to evaluation ratings. As children will have existing diagnoses, no diagnostic feedback will be provided.

We will collect user data (caregiver, clinicians) on satisfaction, ease of implementation, and diagnostic certainty (clinicians only). Based on this feedback, we will modify the preliminary TAP-Preschool instructions and procedures as needed. To systematically measure acceptability and feasibility of use we will utilize an adapted Acceptability, Likely Effectiveness, Feasibility, and Appropriateness Questionnaire (ALFA-Q).[54] The ALFA-Q asks caregivers and clinicians to use a 5-point Likert scale to rate the instrument acceptability, effectiveness, feasibility, and appropriateness for ASD decision making. We will also solicit free-form input. Team leads will briefly interview each clinician and caregiver about their experiences. After each telemedicine evaluation, participating clinicians will view data from previous comprehensive evaluations. Clinicians will provide concrete task evaluation data regarding whether they were able to elicit such behaviors or information in the telemedicine evaluation process. It is important to note that diagnostic agreement rankings will include dichotomous (agree/disagree) and uncertainty data (Likert ratings). As in our previous preliminary feasibility/effectiveness trial, we will target >60% of providers agreeing with existing risk classification for ASD, <10% of ASD inaccurately identified with ASD, and >50% non ASD DD *with certainty* as key benchmarks for understanding potential meaningful clinical value. Based on this data, our investigative team will collaborate with our clinical design team to suggest instrument modifications.

The tele-assessment will take <45 minutes to complete.

The parent forms will take approximately 20 minutes to complete.

Assessment on psychometrics, clinical, and familial value of the TAP-Preschool (Novel Sample):

All consented families will complete an initial home-based tele-assessment visit via Zoom that includes the TAP-Preschool and a brief symptom-focused developmental interview with a consented clinician. The initial tele-assessment session includes interviewing and developmental assessment to mimic real-world use of TAP-Preschool. The visit is designed to take less than 90 minutes, with TAP-Preschool evaluation lasting <30 minutes. Although we will not limit length, we will time all sessions. After the session, the examiner will record the clinical diagnosis issued (ASD, other developmental concerns, or typical development) and complete two diagnostic certainty ratings, one dichotomous, the other continuous. All initial TAP-Preschool administrations will be recorded via Zoom, and 50% of administrations (randomly selected) will be co-scored by a blinded examiner, unaware of prior assessment results and diagnostic decision, to

evaluate inter-rater reliability. Within 7 days of the remote assessment, families will participate in an in-person diagnostic assessment including common comprehensive measures of ASD, cognitive skills, and adaptive behavior. We will randomly select 25% of families to participate in a remote home-based re-test with TAP-Preschool two weeks following initial administration.

Tele-assessment measures: Prior to the appointment, caregivers will complete a *Demographics Questionnaire* (i.e., age, gender race/ethnicity, zip code, parent education) and a *Medical History Form* through a secure HIPAA-compliant web portal (REDCap). To reduce technology-related disruptions, research staff will talk to families before the visit about connectivity settings and recommended materials.

These will take approximately 20 minutes to complete.

In a single tele-assessment session modeled after our previous work, licensed clinicians will administer the *TAP-Preschool,* the *Developmental Profile, 4th edition (DP-4),* and a *DSM-5 ASD interview.* The DP-4 is a caregiver interview (birth – 21 years) that identifies developmental strengths and weaknesses in five core areas. The DSM-5 interview provides symptom-focused questions with developmental anchors pertinent to this age range. Immediately after the session, the clinician will complete a *DSM-5 checklist* indicating symptoms present and clinical diagnosis issued (ASD, other developmental concerns, or typical development). This form also contains dichotomous (certain/uncertain) and continuous (10-point Likert scale) certainty ratings. Clinicians will describe their satisfaction with the tele-assessment process (*CSQ: Clinician Satisfaction Questionn*aire).

The initial tele-assessment appointment with the psychologist will last approximately 90 minutes.

Blinded in-person assessment measures: The in-person examiner will be blinded to the tele-assessment diagnosis until after the in-person assessment. The diagnostic confirmation battery will include the *Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) (one module is chosen based on language ability),* a cognitive measure *(Mullen Scales of Early Learning or Differential Ability Scales 2nd Edition,* the *Vineland Adaptive Behavior Scales, Third Edition*, and a *DSM-5 ASD Interview.* Immediately after the in-person session, the examiner will also complete a *DSM-5 checklist* and certainty ratings.

In-person appointments will last approximately 2-3 hours and will consist of traditional diagnostic evaluations for autism spectrum disorder.

Parent measures: Parents will complete the *Parent Perceptions of Telehealth (PPT)* and the *Parent Service Satisfaction (PSS)* surveys, used in our previous work, to assess perceptions of tele-assessment procedures after the telemedicine and in-person evaluations.

These parent forms will take approximately 10 minutes to complete.

Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others

All members of the research team will be trained and instructed to immediately report any adverse events to the PI. Adverse events will be reported to the IRB within seven days. The PIs, in communication with the study teams, will distinguish serious adverse events (SAE) from non-serious adverse events (AE). The PIs and Co-Is are licensed clinical psychologists with experience establishing adverse event and safety protocols in research projects. All project staff will have training in identifying potential adverse events and reporting procedures.

Should any study participant express concerns about the study or their participation or appear distressed during any study activities, the witnessing research team member will bring the matter to the attention of the PI, or designate at that time, to determine the appropriate course of action, which may include contacting local authorities in the case of imminent danger during a telemedicine appointment (suicidality, child neglect or abuse). Although not anticipated, serious adverse events would be documented and discussed with the IRB as soon as possible and reported to the IRB and NIH project officer within 48 hours.

Study Withdrawal/Discontinuation

Participants can withdraw from the study at any time. If a participant withdraws from the study, research team members will offer other options for having the child evaluated for ASD. If a clinician withdraws from the study they will not be asked to participate again in the current protocol.

Study participation may also be discontinued in the event of repeated technology failures during tele-assessment. Should technology fail (e.g., lost connection that cannot be re-established), we will contact families by phone to schedule a second attempt. If this is also unsuccessful, will document this as part of our ongoing data collection processes while also routing families to appropriate clinical referral pathways.

If a child is in distress (i.e., crying, falling to the floor, shouting) then research staff will take a break and/or consult parents for input/help on how to best soothe their child. The parent will always be given the option to take a break or end the evaluation if they think their child is too distressed to continue.
If a clinician thinks that the child appears to be too distressed to complete the evaluation, opportunities will be given to reschedule the assessment. If the parent declines, the clinician will note that the child was unable to complete the assessment and only data obtained will be included in the study while also routing families to appropriate clinical referral pathways.

Statistical Design and Power

In Specific Aim 2, we will collect user data (caregiver, clinicians) on satisfaction, ease of implementation, and diagnostic certainty (clinicians only). We will examine these data

descriptively (frequencies for satisfaction items; mean/SD for diagnostic certainty) and use them to inform modifications to TAP-P procedures.

In Specific Aim 3, we will benchmark acceptability/usability and preliminary clinical value and then perform rigorous evaluation of the TAP-Preschool relative to in-person evaluation. Our sample size has been determined to power primary analyses around estimates of accuracy, specific psychometric properties, as well as family experience. We will use receiver operating characteristic (ROC) curve analyses to determine a cut score for the optimal scoring method and evaluate characteristics utilizing the entire sample. We will examine agreements and corresponding sensitivity, specificity, and positive and negative predictive value. After estimated attrition of approximately 10%, 108 subjects (projected 65 ASD; 43 non-ASD) will be available for analysis. PPV and sensitivity will have a margin of error no larger than +/- 9.7%, and NPV and specificity will have a margin of error no larger than +/- 12.0%. Margin of error (half the width of a 95% confidence interval) calculations are based on preliminary data from prior data from tele-assessment of ASD and conservatively assuming 80% PPV and 80% NPV. For inter-rater and test-retest reliability, we will be able to measure percent agreement with a margin of error no larger than +/- 7.5% and Cohen's kappa within +/- 0.12. For estimating associations among factors potentially related to clinician diagnostic certainty and caregiver satisfaction, we will have 80% power to detect odds ratios larger than 1.37. All calculations use a two-sided significance level of 0.05 (See Statistical Design and Power for more detail).