STUDY PROTOCOL [VG-Social ABCs]

Parent-mediated intervention for toddlers with early social communication challenges or emerging autism: A multi-site randomized controlled trial of a group-based virtual program that empowers parents as change agents

1. The Need for a Trial

Autism spectrum disorder (hereafter ASD or autism) is a neurodevelopmental disorder with increasing prevalence (>1.5%)[1] and high personal, familial, and societal burdens. Core ASD symptoms include deficits in social communication and interaction (including impaired social-emotional reciprocity and difficulty developing social relationships), and repetitive/restricted patterns of behaviour and/or interests[2]. Many autistic individuals require substantial and costly care across the lifespan from developmental, educational and behavioural services[3], as well as health and mental health sectors[4] due to high rates of comorbid conditions such as anxiety, depression, and ADHD[5-10]. Parental mental health is also often negatively affected, with elevated levels of stress[11], anxiety, depression, and burnout[12]. Access to early intervention can reduce long-term costs[3], but is severely hampered across Canada by long wait times for diagnosis and entry to intervention services. Developing innovative solutions that increase access to earlier intervention and parental supports can mitigate the need for intensive developmental services and later supports, thus reducing down-stream individual, family, and system costs and improving long-term outcomes[3,13].

1.1 What is the problem to be addressed?

Across Canada, toddlers with autism have almost no access to diagnosis-specific intervention due to years-long delays in accessing a diagnosis (i.e., up to two years)[14,15] followed by at least an additional two years' wait to access intervention services in many areas[16]. These delays have only been exacerbated by Covid-19-related isolation measures[17]. This means that the vast majority of high-risk toddlers miss out on early intervention during the narrow developmental window when their brains are most amenable to treatment. Concurrently, parents of children with autism, already at risk for significant mental health challenges[11,12], experience increasing distress as they watch their children fail to achieve key developmental milestones and as they struggle to manage their toddlers' emotional dysregulation associated with core autism symptoms and functional communication deficits. Long-term cascading effects result in children requiring more intensive and/or longer duration of later interventions, with increased costs to the system, coupled with parental hopelessness leading to burnout[12]. This dire situation can be mitigated by capitalizing on ***parent-mediated intervention*** that takes place in the family's home and can be initiated at the first signs of risk for autism (i.e., as early as one year of age[18]). ***Empowering parents to become engaged as the active agents of change for their toddlers, as early as possible, can significantly enhance child outcomes and mitigate parental stress***.

Informed by two decades of longitudinal research with high-risk infants and toddlers[19,20], our team developed and demonstrated the efficacy of a 12-week parent-mediated intervention for toddlers with confirmed or suspected autism (the *Social ABCs*)[21,22]. Co-created with parents and Coaches, the approach operates within a developmental framework, in the child's natural environment, using strategies of applied behaviour analysis (thus a Naturalistic Developmental Behavioural Intervention; NDBI)[23]. By directly targeting the parent-child dyad, the intervention

yields positive outcomes for both toddlers and their parents that are foundational for positive developmental and mental health outcomes: increased positive affect-sharing and social communication in toddlers, and parental empowerment via bolstering their skills and confidence in supporting their children's development (study findings are further detailed below).

1.2 What is the principal research question to be addressed?

In toddlers (aged 18-42 months) with confirmed or suspected autism, is virtual, Group-based intervention using the *Social ABCs* model, more effective than treatment as usual at increasing toddlers' vocal responsiveness to their primary caregivers (i.e., parents)?

1.3 Why is a trial needed now?

Given the rapidly rising prevalence of autism, and significant barriers to accessing traditional interventions, there is an urgent need to develop and evaluate innovative delivery models that can be accessed when the first signs of autism emerge. Promising ways to address this urgent need include (1) involving primary caregivers (hereafter, 'parents') as mediators of the intervention, (2) increasing access via virtual platforms, and (3) providing group-based interventions.
Recent reviews highlight the promise of ***parent-mediated interventions*** for young children with emerging autism, with evidence of gains in key areas of social, communication, and play development[23,24]. A small number of studies have also examined the efficacy of ***virtual parent training methods***, motivated by efforts to increase access. A recent systematic review[25] identified 7 studies of virtual parent-training models, three of which focused on toddlers with autism. Limitations due to weak study design (only 2 studies were RCTs), small samples, lack of measurement of child outcomes, no blinding, and variable or unspecified treatment durations were identified. Only three studies used live, two-way videoconferencing, and only one of these involved toddlers[26], but with a very small sample (n = 8). Despite these limitations, the review concludes that virtual training in parent-mediated intervention "could benefit both parents and children with ASD given the barriers they face in accessing traditional services" [25].
A very recent review of virtual delivery ("video-therapy") in general mental health intervention identifies the rapid increase in virtual intervention in response to Covid-19 isolation measures, highlighting the need for more evidence in support of such approaches[27]. With respect to ***group-based*** video-therapy, the authors conclude that the evidence is even more scant, but extant literature does point to feasibility and "roughly comparable outcomes between in-person and tele-group treatments[27]". Group-based mental health approaches stand apart as being more cost-efficient than individual therapy, and having potential to add unique therapeutic value[28].

Supported by the above evidence, we argue that an innovative and promising approach to increasing access to autism intervention in the very early years involves virtual delivery of a group-based approach to parent training. We are currently pilot testing such an intervention (described below), which is now ready for formal evaluation through a well-powered RCT.
The *Social ABCs* intervention is uniquely well-poised for virtual delivery as evidenced by the initial success of our pilot evaluation (see below). Our model differs substantially from many approaches in its use of a specific set of manualized, active, in-the-moment, supportive parent-coaching strategies that are easily translated to virtual delivery. For example, although used by almost all other parent-mediated approaches, we intentionally *avoid* a training technique called

'modelling' (i.e., working directly with the child to demonstrate strategies to the parent). Our intentional avoidance of modelling was motivated by a commitment to supporting parents to develop their own 'style', to promote positive parent-child interaction, and foster parental empowerment. This unique coaching stance, shown in our previous work to successfully promote parent skill acquisition and self-efficacy, makes the *Social ABCs* ideally suited to virtual delivery. The ***virtually delivered Group-based model***, proposed for the current evaluation, is an adaptation of our original (12-week, individual, in-person) *Social ABCs* program. Our original model has been shown to be feasible and acceptable[21], and a cross-site RCT[22] demonstrated improvements in toddlers' communication skills (i.e., significant gains in toddler vocal responsiveness and initiations; *p*'s < .001), parent positive emotion-sharing ($p = .017$; which predicted gains in child smiling), and a trend toward increased toddler social orienting ($p = .054$). Parents learned the techniques (i.e., fidelity >80%) and reported increased self-efficacy ($p = .009$)[22]; qualitative analyses of parent interviews revealed themes of empowerment and hopefulness[29]. We have also now successfully completed a large community implementation ($n = 183$)[30-33], with effectiveness commensurate with efficacy shown in our initial RCT, across a wide range of parent factors (gender, English language learner status, educational attainment [ranging from grade 9 to graduate school completion]) and child variables (age, sex, language skills)[32]. We have made two key adaptations to the original model, with promising pilot findings (described in section 2.19).

1.4 How will the results of this trial be used?

This project addresses the acute developmental and mental health needs of individuals with disabilities, as well as their families, identified by KBHN and CIHR as priority populations. Outcomes will establish the evidence needed to fill an urgent gap in the system –increasing access to treatment for toddlers at the first signs of risk by empowering parents as the agents of change.

In most Canadian jurisdictions, ASD service funding is very difficult to access under age two. Moreover, there is a complete lack of funding/services specific to the needs of toddlers with emerging signs of ASD who do not yet have a confirmed diagnosis. There is a traditional care pathway of generic followed by diagnosis-specific intervention that misses opportunities for more targeted approaches. Similarly, there is a chronic gap, in publicly funded community service models, between early detection and early intervention that does not reflect the state of current evidence (i.e., we can identify the early signs, but despite the existence of evidence-based interventions, there is little that parents can access when initial signs are identified).

Results from this trial will contribute evidence that can be used to make the case for very early intervention as soon as autism-related concerns arise. Exploratory examination of factors related to feasibility and acceptability will inform future implementation work. Our research is embedded in community-based clinical intervention programs, with training partnerships across Canada (e.g., McMaster Children's Hospital, Children's Hospital of Eastern Ontario, and Glenrose Rehab Speech-Language services in Alberta) and ongoing collaborations in India (Sethu Centre for Child Development in Goa, as part of the Indo-Canadian Autism Network Symposium; see www.socialabcs.ca for details) and in Israel (in collaboration with The Hebrew University; see www.autismchildfamily.com for details).

Knowledge mobilization will involve engaging Holland Bloorview's Evidence-to-Care team to co-develop lay summaries, and support uptake of research findings into practice. We will share study findings through scientific conferences and community meetings (e.g., Infant Mental Health Promotion, Canadian Paediatric Society (CPS), infant development, psychiatry and psychology training programs, and relevant provincial ministries). Team members' leadership roles within professional associations and relevant policy-advisory groups (see CVs and Most Significant Contributions) will provide platforms through which to share findings and influence provincial policy and national practice. Our team has an established record of translating empirical findings into clinical practice (e.g., CPS practice statements, 2019; www.cps.ca/en/documents/tag/autism).

1.5 Are there any risks to the safety of participants involved in the trial?

We have delivered the *Social ABCs* intervention to over 300 families (across our initial pilot study, two RCTs, community implementation work, and our current pilot evaluation of the in-person and virtual Group models) without any significant adverse events. Use of a virtual platform presents potential risks associated with breach of privacy (mitigated by the use of *Zoom for Healthcare* which is compliant with Canadian healthcare privacy and security regulations). Risk of miscommunication or of missing out on important indicators of mental distress may also be elevated. However, "seeing" more of the family/home circumstances may also provide increased information that would guide the need to follow up regarding mental health or social supports. As with in-person intervention trials, our team is equipped to support parents who express distress (often associated with this early phase of identifying their young child's developmental challenges) via providing supportive advice, offering families access to local team leads (all with clinical credentials), and/or helping families navigate community mental health resources, as appropriate. Notably, our parent-mediated intervention (which might be viewed as placing extra demands on parents) did *not* lead to increased stress in our original RCT[22].

1.6 How will potential participants learn about the study?

The study team will prepare recruitment letters (to be approved by REB) and will share these electronically with community leaders and clinicians both within and outside of the main study centres (Holland Bloorview, Glenrose Rehab, and the IWK). These letters will be sent at the beginning of our recruitment period, and the clinicians receiving the information letters will share them with potential participants at the time of clinical care. This is the same process that we have used for recruitment in our previous and ongoing studies and it has worked very well. Families are given the recruitment letters and they may call our team if interested in participating or learning more.

2. The Current Trial

2.1 What is the trial design?

This is a multi-site, single-blind, randomized group treatment trial. Participants are subjected to three design components (further detailed below): (1) parallel group design with a treatment and an active control arm, (2) own-control (within subject) design for the control arm after these

participants receive treatment (control-treatment), and (3) growth curve analysis of treatment group at *Time 0* (baseline), *Time 1* (after treatment), and *Time 2* (follow-up).

2.2 What are the planned trial interventions?

Once consent is obtained, baseline (*Time 0*) video and questionnaire data are collected and then allocation to treatment arm is revealed. In cases of allocation to Arm A, an assigned Coach meets with each family to discuss family scheduling preferences for coaching sessions, technology issues, and child skills/interests, and then intervention begins.

Arm A. The ***intervention*** is the ***Group Social ABCs, adapted for virtual delivery (VG-Social ABCs)***. The intervention will be provided to small groups of parents (4-8 per group) who meet virtually for a series of six didactic learning sessions led by two Coaches, supported by our **Parent Manual** available in English and French; although all coaching will be in English), PowerPoint slides and involves facilitation discussion, reflection, and idea generation. Each family is assigned a Coach, and one parent per family will receive nine individualized, 1:1 coaching sessions over a 6-week period ***via the virtual platform*** (see Appendix A for study sessions). Parents will participate in an introductory virtual session at which the Coach introduces the aims and structure of the program, discusses family scheduling preferences, technology issues, and child skills/interests, obtains research consent, and collects a ten-minute pre-coaching video recording of the child interacting with the parent (*time 1*); baseline questionnaires are completed at this time as well. Following the 6-week intervention, a second parent-child interaction video is taken (*time 2*) and post-intervention questionnaires are completed by the coached parent; a follow-up video is collected at *time 3* (see below). For all video recordings, parents are instructed to: "*play with your child as you typically play, and try to capture both you and your child on the video*". Videos will be collected over the virtual platform, saved to virtual drives within institutional firewalls, and shared securely for video coding, based on formal data sharing agreements. Parent Coaches will be existing *Social ABCs* Coaches from all three sites (with backgrounds in Psychology, Early Childhood Education, Speech-Language Pathology, or Applied Behaviour Analysis), all with substantial in-person parent coaching experience, recent virtual coaching experience, and cross-site reliability. Our team will meet regularly to ensure consistency of virtual coaching practices and for supervision, using case-based video review per our longstanding model of cross-site reliability and clinical supervision. During this phase, families will be asked to limit other interventions to 1 hour/week each, as per our current protocols. See Appendix B for contents and selections from Parent Manual and Coaching Manual.

Arm B. The ***active control*** condition controls for the co-intervention of group-based general support (i.e., regular contact with a supportive facilitator, interaction with other families), but without the 'active ingredient' of parent coaching that is fundamental to the *Social ABCs*. This condition involves three, bi-weekly (virtual) group-based sessions (i.e., groups of 4-8 parents, over 6 weeks) with a psychoeducational curriculum delivered by study personnel and Psychology graduate students not directly involved in the *Social ABCs* sessions. Families may access any available services in their communities (i.e., treatment as usual), which are recorded on our *ST Form*[24]. Given the current (extremely limited) availability of community early interventions and the brevity of the study, we anticipate that families will have limited access to other intervention while in the control condition (e.g., families in our previous study accessed < 1 hour/week of

"other" interventions over 6 months[24]). Families will be offered the *VG-Social ABCs* program after completing Arm B. Despite some concern that a waitlist control design can exaggerate treatment effects[37], we feel ethically driven to offer the program after participation in the control condition. Moreover, the inclusion of a waitlist component to the active control condition may *lessen* the treatment effect, strengthening our confidence in positive findings. Data collection and time-points are the same as for the intervention arm (Arm A).

2.3 Proposed practical arrangements for allocating participants to trial groups.

Third-party randomization will be conducted. Random block sizes of 10 participants will be used for treatment assignment. There will be 12 blocks of each size for a total of (10*12) 120 participants, 60 participants per treatment arm (5*12=60), drawn to account for 20% loss to follow-up eight blocks (8*10=80) for n = 100 in each arm. A trickle process will allow for sequential enrollment[36].

2.4 Proposed methods for protecting against sources of bias.

This is a single-blind study. Blinding of families and Coaches to group assignment is not possible given the nature of the intervention, which is delivered by Coaches and mediated through parents. However, video coders, who will collect data for the primary outcome (and many secondary outcomes), will be blind to both treatment allocation and time (pre-intervention, post-intervention, follow-up).

2.5 What are the planned inclusion/exclusion criteria?

Inclusion Criteria. Eligibility will be based on elevated scores on the Autism Parent Screen for Infants (APSI[37]) supported by expert clinician impression of red flags for autism spectrum disorder (ASD), or a confirmed diagnosis of ASD made by a qualified professional (parents will be asked to provide the clinical report). Toddlers will be between ages 12 and 42 months at enrollment, having been born between 36 and 42 weeks' gestation, with birthweight >2,500g and no neurological, genetic, or severe sensory or motor conditions. Participating families must be residing in Ontario, Nova Scotia, or Alberta at the time of participation.

Requirements for participation include ability to comprehend verbal English instructions. Our Parent Training Manual is written at a grade four language level, but concepts are shared verbally and through images, so literacy is not a requirement. Participation is also dependent on access to high-speed internet and willingness to be video-recorded, for cross-site consistency checks and data acquisition. Parents will be asked to limit other social communication intervention programs (e.g., through Speech-Language Pathology, Occupational Therapy, Applied Behaviour Analysis, or related services) to 1 hour per week. Parents will also complete weekly services log to document involvement in such programs. Finally, parents will be encouraged to try not to miss more than 2 sessions in a row. Missed sessions will be rescheduled if possible. However, all families will be invited to provide end-of-study data even if multiple sessions are missed (number of sessions attended will be used as a covariate in analyses). Families may withdraw at any time.

There are no ***exclusion criteria*** other than failure to meet inclusion criteria.

2.6 Proposed duration of treatment period.

Treatment duration is 6 weeks. Time span between data collection time points will range from 7 to 9 weeks to allow for re-scheduling if necessary.

2.7 Proposed frequency and duration of follow up.

Data will be collected for both groups at: baseline (*Time 0*), 6 weeks later (*Time 1; within 6-8 weeks*), and following the next 6 weeks (*Time 2; within next 6-8 weeks*). Time 2 for the treatment group provides follow-up data to examine maintenance of gains in our primary outcome (toddler vocal responsiveness) and parent fidelity.

2.8 What are the proposed primary and secondary outcome measures?

Primary Outcome: Toddler vocal responsiveness (blind video-coded).
Secondary Outcomes: *1. Toddler outcomes:* (a) vocal initiations, (b) social orienting, (c) words understood and used, (d) autism symptoms; *2. Parent outcomes:* (a) implementation fidelity, (b) self-efficacy, (c) stress.

Exploratory Analyses: *1.* ***Predictors****:* Child factors (e.g., sex assigned at birth, age, baseline language level, ASD symptoms) and parent/family factors that may influence outcomes (e.g., parent gender, parenting role, educational attainment, employment, stress, ethnicity, English spoken at home, family structure)[40]; *2.* ***Implementation metrics****:* Feasibility and acceptability (see below).

2.9 How will the outcome measures be measured at follow up?

Primary Outcome: Toddler vocal responsiveness. Consistent with our previous work[21,22], video coding will be used to measure toddlers' vocal responsiveness (proportion of appropriate child vocal responses following a caregiver prompt, from 10-minute video). All video coding will be conducted by blinded research staff with established reliability, per established protocols. ***The primary outcome is change in toddler vocal responsiveness from time 0 to time 1***.

For all parent-child interaction videos**, parents are instructed to: "*play with your child as you typically play"* and reminded that: "*we want to see both of you on the screen as much as possible"*. **Two 10-minute video clips** will be collected and coded per time point (using average per time-point for analyses); **no coaching occurs during data videos**. Videos will be collected by research staff over the virtual platform, saved to virtual drives within institutional firewalls, and shared securely for coding, based on formal data-sharing agreements. ***Blinded research staff with established inter-rater reliability will code all videos, per established protocols.

Secondary Outcomes (all measures used in our previous and/or ongoing work)**:**
1. Toddlers. (a) Vocal initiations and (b) social orienting (both blind-coded from video); (c) parent-rated word inventory (MacArthur-Bates Communicative Development Inventory [CDI][38]); (d) autism symptoms (APSI[37]). *2. Parents*. (a) Correct use of *Social ABCs* strategies (%

implementation fidelity from blind-coded video), (b) self-efficacy (Parent Self-Efficacy Scale[22] developed for our previous work), (c) parenting stress (Parenting Stress Index-4-Short Form[39]).

Exploratory Analyses:
*1. **Predictor variables**:* Continuous (parenting stress, child age, baseline word inventory, ASD symptoms) and categorical (toddler sex, parent gender, parenting role, educational attainment, employment, ethnicity, English spoken at home, family structure), variables (collected from the *Family Profile Form*[24]) will be assessed for their effect on the outcomes; *2. **Implementation metrics**.* We will measure *acceptability* using our post-treatment Parent Satisfaction Scale[22], and a Coaches' Satisfaction Scale (under development) to capture Coaches' perceptions of the adapted model relative to the standard approach. Program *quality metrics* will include evaluation of Coaches' fidelity (based on pre-established video-coding methods). We will examine *participant flow* metrics such as referral sources, ages of children, and number referred, eligible, enrolled, and completed, as well as number of sessions attended/missed/rescheduled.
2. Sub-group and predictor analyses will explore child factors (e.g., age, sex, baseline language level) and family factors that are facilitators or barriers to treatment uptake and successful outcomes (e.g., parents' educational attainment, current employment, family structure, parent gender)[40], using data collected from a Family Profile Form used in our previous work[22].
3. Follow-up (treatment group only). A 10-minute parent-child interaction video will be collected and coded for toddler responsiveness and parent implementation fidelity using the same procedures as for *time 1* and *time 2*.

2.10 Proposed sample size and justification for assumptions underlying power calculations.

We aim to enroll 120 families into the RCT, across the three participating sites.

This project has two phases, differing only by number of participants and funding source. Specifically, phase 1 (funded by Kids Brain Health Network) involves enrollment of 30 families across the 3 participating sites. For phase 2, funds are being sought through CIHR (to be adjudicated in March 2021). If funded, we will submit an amendment to increase recruitment up to 100. The proposed sample (n = 100; ~50 per treatment arm) will yield 80% power to detected a medium effect (at alpha = .05)[41]. The assumption of a medium effect comes from our previous RCT which yielded R^2 = .43 for the same primary outcome[22]. We will over-sample by 20% (i.e., recruit to n = 120) to allow for attrition (see 2.14). Given that this is an individually randomized group treatment trial (with 1 group-based and 1 individually administered arm) analyses will account for the intra-class correlations associated with group participation, as recommended[34]. If Phase 2 is not funded, we will use data from Phase 1 as pilot data for further funding applications.

2.11 If applicable, will health service research issues be addressed?

This is not primarily a health services proposal. However, exploratory investigation of issues related to feasibility (# of families invited, enrolled, completed) and acceptability (via parents' satisfaction ratings) will inform future implementation work. Our ongoing KBHN-funded work focuses on training and community implementation, including health economics analyses, with ongoing consultative support from M Barwick (Senior Scientist in the Department of Psychiatry and Child Health Evaluative Sciences program at SickKids' Research Institute in Toronto).

2.12 Planned recruitment rate, organization, time period.

Families will be recruited from our three collaborating sites through clinical and research units and community partners. Recruitment will begin in Year 1 (2nd quarter; Q2) and conclude in Year 3 (end of Q1), allowing sufficient time to code and analyze data for manuscript preparation in Year 3 (see Timeline in Appendix C). Per regional populations and enrollment rates in related work, expected recruitment rates are as follows: (Toronto: 50, Edmonton: 40, Halifax: 30). Recruitment is anticipated to be successful based on the current pilot phase (i.e., the number of interested families currently far exceeds our capacity to enroll them). All three sites have been recruiting high-risk infant siblings of children with autism for longitudinal studies for almost two decades, and are thus well known in our respective communities and have established recruitment pipelines through community partners.

2.13 Are there likely to be any problems with compliance?

We will measure both program compliance and treatment fidelity. **Compliance** rates will be measured by the number of training sessions attended. As in our previous and ongoing work, families will be permitted to miss and reschedule up to 3 individual coaching sessions. Families who miss up to two group didactic sessions will receive session content in a subsequent 1:1 session with their coach. Since the program does not require families to use the strategies for any pre-specified amount of time per day, attendance is our best measure of compliance. However, our established measure of parent implementation **fidelity** provides an index of parents' skill acquisition which serves as a proxy for their amount of practice. In our RCT, 87% of families in the treatment condition achieved our target fidelity rate by the end of the program[19].

2.14 What is the likely rate of loss to follow up?

Retention rates of 85-90% are expected, based on our previous RCT[22] and current pilot work. In the initial RCT, >90% of families remained at 6-month follow-up (Treatment: 90.3%; Control: 93.8%). Retention in our pilot evaluation of the virtual Group-based model is currently at 86% (19 of 22 have completed the program). Retention rates are anticipated to be similar to previous rates and may be further supported by the virtual nature of the project (i.e., families do not have to travel to participate). However, due to uncertainties associated with family availability (e.g., in response to Covid-19-related changes in work stoppages or isolation practices), we will over-sample to 120 to ensure we reach our target of 100 completers.

2.15 How many centres will be involved?

Three collaborating sites across Canada: Holland Bloorview (Toronto, ON), IWK Health (Halifax, NS), and Glenrose Rehab (Edmonton, AB).

2.16 What is the proposed type of analyses?

The primary analysis will yield a comparison of rates of toddler vocal responsiveness between the two conditions, controlling for the variables described above. The statistical model for the

Primary Outcome will be either a Poisson or negative binomial regression (if there is overdispersion of the counts), using the number of prompts and/or time as offsets and applying the appropriate correlation structure for observations by participant, and controlling for intraclass correlation due to clustering. Growth curve analysis will be used to calculate the trajectory of change in responsive vocalizations over time for each person based on whatever data are available (if at least 2 measurements), and then estimates (imputes) the missing data if the person followed the same trajectory. Otherwise, a worst-case (no vocal response) scenario can be used.

Secondary Outcomes: We will analyze as per the primary outcome for count variables (e.g., video-coded toddler initiations). We will use repeated measures ANOVA or Generalized Estimating Equations for scores (e.g., word inventory, ASD symptoms, parent efficacy, stress).

Exploratory Analyses: *(1)* ***Predictors*** of primary and secondary outcomes will first be assessed univariately for their effect on the outcomes, and significant factors will be subjected to multivariate analysis using the appropriate regression model. We will examine the influence of sex (toddlers), parent gender, and parenting roles by entering these factors as covariates. Given that sample size calculations are not done for all these factors, these analyses are exploratory. (*2)* ***Implementation metrics*** (feasibility, acceptability) will be examined descriptively.

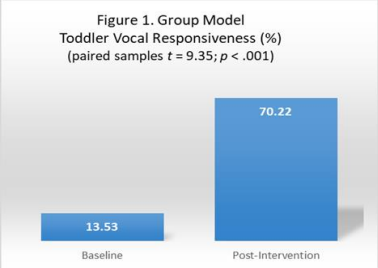
2.17 Proposed frequency of analyses. Analyses will be conducted at two time points: (1) following the end of Phase 1 (n = 30), and (2) at the end of the larger trial (n = 100).

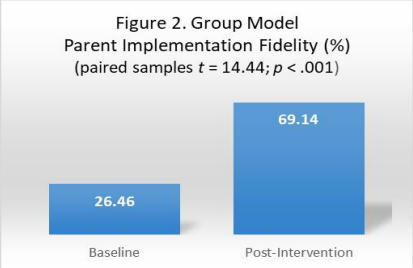
2.18 Planned subgroup analyses.

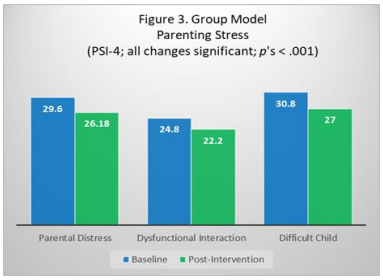
Subgroup analyses, run separately for treatment and control groups, will explore effects of: (1) sex*: Do outcomes differ for boy vs. girl toddlers?; (2) gender: Are there differences in parent fidelity and self-efficacy based on self-identified parent gender?; (3) baseline language functioning: Do outcomes differ for toddlers who begin the program below (vs. at or above) a 12-month language level (based on parent-reported CDI scores)?*

2.19 Has any pilot study been carried out using this design?

We have made ***two substantive adaptations to the standard Social ABCs program***, each with some pilot data. First, we developed a **Group-based** protocol for didactic learning and shortened the duration of 1:1 coaching (6 vs. 12 weeks). We have pilot tested the Group adaptation (n = 45 in-person families) with positive reports from families and Coaches (see *Report to Alva Foundation*, attached). Preliminary analyses[43] reveal significant gains in toddler responsiveness and parent fidelity comparable to those for the original model (see Fig. 1 and 2). Unique to the Group model is evidence of ***reduced parenting stress*** (Fig 3), which highlights the enhanced clinical impact of a Group-based intervention that goes beyond increased efficiency[28]. Parents in the Group model also reported improved toddler language (words understood and spoken[38] significantly increased, p's < .001), reduced toddler autism symptoms (APSI[37] scores decreased significantly from 20.5 to 17.2; p = .0005), and high satisfaction (33.1 out of a possible 35).







The second key adaptation to our original model involved developing a **virtual coaching protocol** for the Group model. Our team made this additional adaptation in April 2020, in response to the Covid-19 pandemic, ***and we have already piloted this adapted virtual Group model with an additional 22 families*** *(and 11 in progress),* demonstrating the feasibility and promise of this novel approach. Preliminary analyses of the ***virtual Group-based adaptation*** reveal outcomes similar to the *in-person Group model*, with comparable gains in parent fidelity (from 30.8% to 72.2%; $p = .009$) and a trend toward reduced parenting stress (from 31.8 to 25.5) similar in magnitude to the in-person values. Although child-level video data have not yet been coded, parent-reported autism symptoms (on the APSI[37]) decreased significantly (23.2 to 18.5; $p = .004$), and satisfaction was high (32.5 out of 35). Parent-reported toddler language also increased (p's = .003, .018, respectively for words understood and spoken). ***On all metrics evaluated to date, changes are commensurate across in-person and virtual delivery methods.***

The ***adapted, virtual group delivery model*** is a promising, innovative and cost-efficient way to provide intervention to toddlers with probable or confirmed autism at the first signs of concern.

3. Trial Management

3.1 What are the arrangements for day to day management of the trial?

The team already has procedures in place to facilitate trial management; we have access to a senior Research Coordinator (RC), experienced in clinical trials management on multi-site intervention trials. She will oversee registration of the trial with clinicaltrials.gov and management of cross-site collaboration to ensure consistency and compliance. The central RC will assign randomization codes and ensure blinding of videos in preparation for coding. We have a full complement of trained Coaches and Research Assistants at each site. Because the project is ***entirely virtual***, we do not anticipate any study delays or stoppages related to current or future Covid-19 measures.

3.2 What will be the role of each principal applicant and co-applicant proposed?

Nominated Principal Applicant: **J Brian** PhD is a clinical-developmental psychologist and clinician-investigator with extensive expertise in early ASD characterization, family support, and intervention. She will lead all aspects of project development, realization, interpretation, and knowledge mobilization (2 days/week on this project). Dr. Brian led the cross-site RCT[22] of the original model, currently co-leads a multi-site attention co-intervention RCT (analyses underway), and collaborates on several RCTs investigating pharmacological treatments in autism.

Co-Applicants: **IM Smith** PhD (Halifax Lead), psychologist, will oversee and supervise program delivery, data collection, and video coding at the Halifax site. She will contribute considerable expertise in community-based ASD early intervention research, and will contribute to interpretation of study findings and manuscript preparation (.5 day/wk). **L Zwaigenbaum** MD (Edmonton Lead), developmental paediatrician, will oversee and supervise program delivery and data collection at the Edmonton site. He has expertise in research design and biostatistics, early ASD detection, and community partnerships to facilitate uptake into care. He will contribute to statistical analysis, interpretation, and manuscript preparation (.5 day/wk). **P Andreou** PhD is a Biostatistician at Dalhousie University with expertise in clinical trials, sample surveys, and statistical modelling. He will be responsible for issues related to trial design, randomization, analyses, and interpretation (.5 day/wk at study initiation and year 3 analyses and interpretation).

Collaborators –Knowledge Users (KUs): KU's represent organizations that currently use or are interested in implementing the Social ABCs if the trial shows positive effects, and community stakeholders who can advise on implementation considerations. **C Roncadin** PhD, clinical psychologist and Clinical Director ASD services; **I Drmic** PhD, clinical psychologist in mental health and autism (both McMaster Children's); **D Chitty** PhD, clinical psychologist and Provincial Leader for Nova Scotia (NS) Early IBI, and **N Beswick** MSc-SLP, Speech Language Pathologist/ Clinical Lead Pediatrics; Communication Disorders (Glenrose Rehab, AB. Annual stakeholder meetings with KUs, steering committee members, and family advisors will occur virtually to review study progress and to advise on implementation factors (e.g., participant flow, feedback). See letters of support from additional community stakeholders (attached).

Family Advisors: **S Cosgrove** and **A Zarem**, both with considerable experience on family advisory boards, will each bring a unique parent perspective to stakeholder meetings, interpretation of findings, and idea-generation regarding future wide-scale implementation; one family advisor will be invited to join the steering committee. *Program Partner:* We have secured funds from Kids Brain Health Network (KBHN; see partner letter) to support this project *(n=30)*. We will leverage these funds to supplement the current proposal and reach our recruitment target. *Consultation:* **S Bryson** (Professor Emerita, Dalhousie U), program co-developer, will support interpretation of findings and manuscript preparation.

3.3 Trial steering committee and data safety and monitoring committee.

The ***steering committee*** will consist of J Brian, IM Smith, L Zwaigenbaum, two senior Coaches (E Dowds and K Bernardi), and one family advisor, and will meet formally every six months throughout the project, with ad hoc meetings as needed. Statistical analyses will be conducted by J Brian and L Zwaigenbaum, with consulting support through the University of Toronto (OISE) statistical support service. Despite low anticipated risk, we will establish a ***data safety and monitoring board*** using processes in place in our current work, with members external to the conduct of the study: one scientist, one member with biostatistics expertise, and one family advisor (different from those named above). This committee will meet twice yearly to review enrollment, completion, and withdrawal rates, adherence to the study protocol, protocol violations or deviations, any adverse events (which are also reported to our Research Ethics Boards), and external factors that might affect the ethics of the study.

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