A feasibility randomised controlled trial on the efficacy of the WHO's 'Caregiver Skills Training programme'

Statistical Analysis Plan

ISRCTN: 58638141

Description of the trial

This study will assess the feasibility of a randomised controlled trial (RCT) with a 1:1 allocation ratio to a Caregiver Skills Training (CST) intervention group and a control group. The CST intervention is composed of multiple components delivered over a period of approximately 4 months: 9 Group Sessions, 3 Virtual Home Visits, and 4 Telephone Calls over the course of the intervention period. Families will be enrolled in 4 blocks of 20 caregivers in each block, for a total of 80 families. Half will be randomized to receive the intervention and the other half in the control group. Families in the control group will be offered intervention after a waiting period that corresponds to the completion time of the CST programme.

Research objectives

The overall aim of the study is to examine the extent to which the Caregiver Skills Training (CST) programme trial can be feasibly implemented in the study setting. Specifically, we aim to fulfil the following objectives:

Primary objective:

- Feasibility and adherence: obtain estimates of participant recruitment and retention rates, data completeness/adequacy, and intervention adherence.

Secondary objectives:

- Obtain preliminary effect estimates of CST on caregiver-child interaction, child language, child emotional and behavioural problems, caregiver distress and caregiver empowerment to power a future large-scale trial.

Trial design

Figure 1 shows the trial flowchart with various stages of the trial and Table 1 details the assessment tools used in each stage. REDCap system will be used to support data capture and monitoring forms for questionnaires, direct assessments, and delivery of the intervention.

Figure 1. Template CONSORT diagram

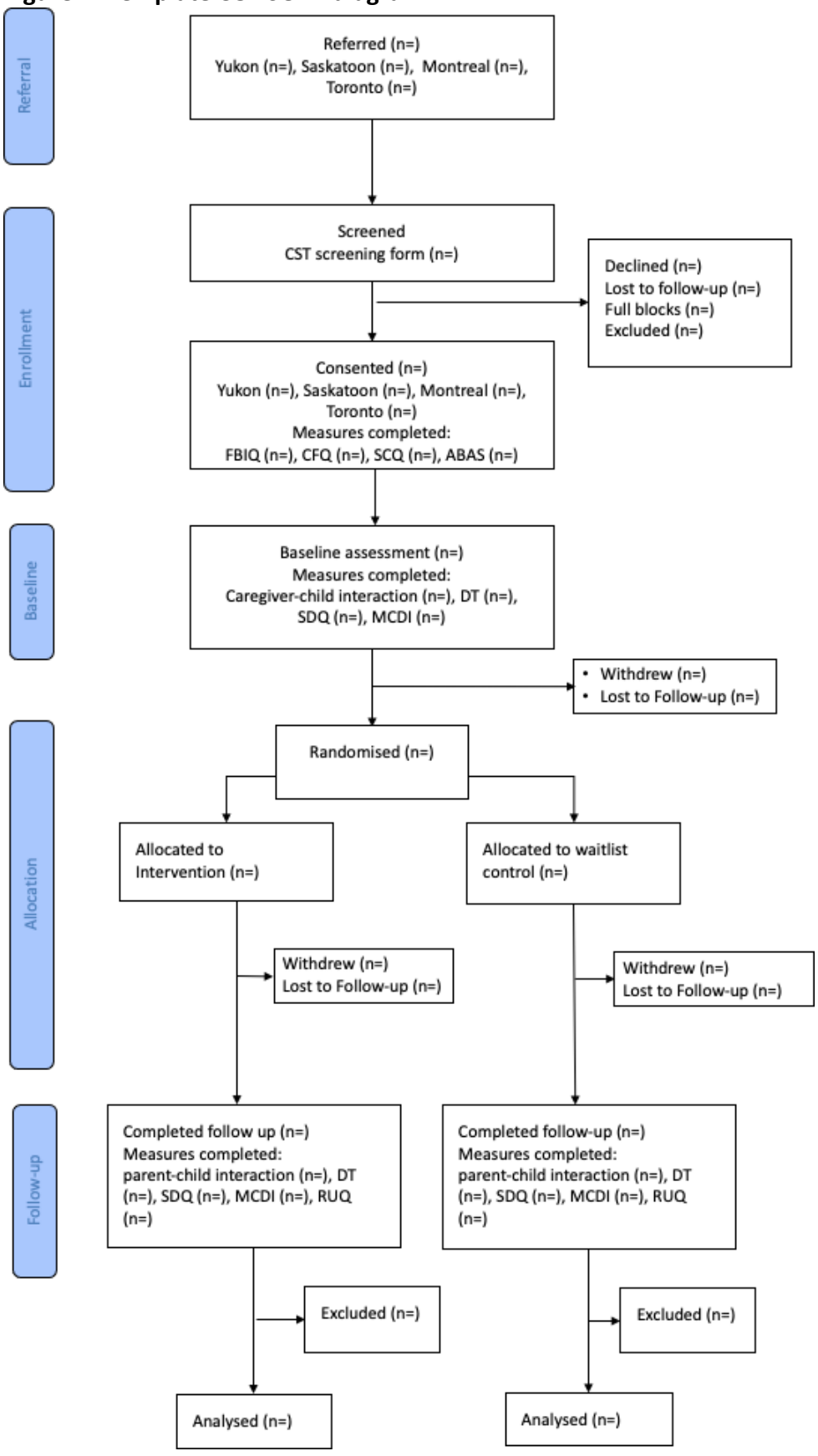

Table 1: Assessment tools with time of collection and variables specified for summary/analysis in SAP

Measure	**Enrolment**	**Baseline**	**Interventio**	**Follow-up**	**Variable extracted**
CST Screening Form	X				• Number of sites referring to the study • Number of caregivers referred by each site • Number & proportion of caregivers eligible • Child chronological age
CST Consent Form for Caregivers	X				• Number & proportion of caregivers consented
Randomization Form	X				• Number of participants randomised by trial arm
Withdrawal Form	X	X	X	X	• Number of participants who withdraw
Family Background Information Questionnaire (FBIQ)	X				• Child Biological sex • Language exposure • Family income
Children in Family Questionnaire (CFQ)	X				• Number of siblings
Social Communication Questionnaire (SCQ)		X			• Total Social Communication Score
Adaptive Behavior Assessment System 3rd ed (ABAS)		X			• General Adaptive Composite (GAC) score
Resource Use Questionnaire for Preschoolers (RUQ-P)				X	-
Caregiver-child Interaction Assessment (coded with the Dyadic Communication Measure for Autism (DCMA)		X		X	• Frequency completed • Parental synchrony • Child initiations
Distress Thermometer		X		X	• Frequency completed • Caregiver distress
Family Empowerment Scale		X		X	• Frequency completed • Family subscale total score
Strengths & Difficulties Questionnaire (SDQ)		X		X	• Frequency completed • Total difficulty score
MacArthur Communicative Development Inventories (MCDI)		X		X	• Frequency completed • Total number of words produced
CST Consent Form for Interventionists	X				-
MT Feedback Form			X		• Number/proportion of participants attending all 9 Group Sessions • Average number of Group Sessions attended

CST Remote Home Visit Guide			X		• Number and proportion of CST participants completing all 3 Virtual Home Visits • Average number of Virtual Home Visits attended
CST Telephone Calls Guide			X		• Number and proportion of CST participants completing all 4 Telephone Calls • Average number of Telephone Calls completed
CST Adult-Child Interaction Fidelity Rating			X		• Total fidelity rating score
CST Caregiver Diary			X		-

***Referral*:** Participants will be recruited from one of five sites across Canada (McGill University Health Centre, Douglas Mental Health University Institute, Autism Yukon, Autism Services of Saskatoon, and South Asian Autism Awareness Centre). Referring professionals at recruitment sites will identify potential participants and present families with a flyer about CST. Registries and other recruitment methods may be also used. Potentially eligible participants will receive a link to complete the CST Referral form to consent for contact by the research team.

***Enrolment*:** The research team will provide consent forms and study information flyers to potential participants either electronically or by mail and assess eligibility. A Screening form will be used to assess the following **Eligibility criteria:**

1. The child is aged between 2 to 7 years; 11 months,
2. The child is suspected of or diagnosed with ASD, a global developmental delay, an intellectual disability, or any other related neurodevelopmental condition,
3. The child is either pre-verbal or has language abilities that are lower than what is expected for their age, i.e., no more than 3 words in length,
4. The primary caregiver, i.e., the individual responsible for the daily care and upbringing of the child, including parents, grandparents, or any other adult over the age of 18, can attend all relevant assessment and intervention activities.

Participants will be excluded if they meet any of the following:

1. Child is already enrolled in an intensive treatment program (more than 14 hours a week)
2. Any factor interfering with the caregiver's ability to complete the program; for example, limited knowledge of English; limited or unstable contact with the child; no access to a computer, tablet or laptop, or a secure internet connection.

Eligible caregivers will be consented to their own and their child's participation in the study. A number of demographic and clinical characterization measures outlined in Table 1 will be collected.

***Baseline*:** Once a block of 20 families have been consented, 10 families will be randomised to receive the CST Programme right away and 10 will be randomized to a wait-list control (treatment as usual). Enrolled participants will complete the measures outlined in Table 1.

***Allocation*:** Once eligible participants have consented, caregiver-child dyads will be randomly allocated to either the immediate CST or control group with a 1:1 ratio and stratified by preferred language (English vs. French in the Quebec sites). Simple randomisation will be performed using random numbers programmes in R-CRAN (version 3.3.0) by an assigned team member who is not involved in the study in any other capacity.

The numbers generated and the randomisation will only be accessible to this team member to ensure concealment. The randomisation procedure will begin once all the families for each block have been recruited.

Participants in the intervention group will receive the CST intervention immediately following enrolment (9 group sessions, 3 home sessions, 4 phone calls). At that time, the waitlist control group will only have access to CST intervention materials, namely the Participant Booklets then wait to receive the full interventions 4-5 months after randomization. Trained interventionists who will offer CST to participating families (called Master Trainers) will also read and sign a consent form to be returned to the research team either electronically or by mail. A number of measures will be collected by the Master Trainers and by the research team to examine intervention adherence and fidelity of interventionists while they deliver CST to both the experimental and control groups.

Follow-up: After the first group of 10 families allocated to the intervention have completed the intervention, all 20 families will undergo follow-up assessments as outlined in Table 1.

Blinding: Due to the nature of the intervention, neither the interventionists nor the families can be blinded to allocation. Every effort will be made to ensure that outcome measures are administered by the research team who are not involved in the intervention delivery and are blinded to treatment allocation. The research team will enter data directly into the online data collection platform to ensure that data monitoring can occur without unblinding. Group assignment will not be revealed until the end of the study after database lock.

Sample size estimation

In line with guidance on feasibility studies, no power calculation has been carried out (Arian et al., 2010). A sample size of 60 to 100 has been shown to be sufficient in a feasibility trial (Moher et al., 2001). A target sample size of 80 (N=40/arm) will be enrolled and randomised based on the practical number of participants who can be recruited to undergo the CST programme at each recruitment site considering the available resources at each recruitment site.

Data monitoring

After the completion of the first programming block, a brief data check will be conducted by an independent analyst. The analyst will request pooled data extracts (no information on participant treatment allocation) to analyse and report the following:

- Summary of numbers initiating the enrolment/intake stage, consented, completing baseline, randomised, and those completing follow up
- Descriptive statistics for baseline demographic measures
    - Frequency and proportion of missing data for demographic variables
- Descriptive statistics at baseline and follow up for caregiver-child outcomes
    - Frequency and proportion of missing data for each measure at both timepoints

Descriptive statistics for baseline demographic measures will be produced for the set of those randomised. By request of the trial team, demographics for all those considered screened will also be summarised descriptively.

Statistical analysis plan

Demographic and clinical characteristics

To describe the study sample and check that the trial arms are balanced, demographic and baseline variables will be summarised by trial arm and across the total study sample. The following variables will be extracted from the Enrolment measures (Table 1):

- Child chronological age (continuous)
- Child Biological sex (categorical: male, female, or intersex)
- Language exposure (mean exposure to testing language at home and school, two items item scored 1 = very rarely to 5=always)
- Family income (binary: Below $60k average household income versus above)
- Number of siblings (continuous)
- Total Social Communication Score (continuous)
- General Adaptive Composite (GAC) score (continuous)

Summary statistics will be calculated (means and standard deviations for continuous outcomes if normally distributed, medians and quartiles if skewed; frequencies and proportions for discrete outcomes). The randomisation of intervention groups to participants should have ensured that any imbalance over all measured and unmeasured baseline characteristics is due to chance. Therefore, no significance testing will be conducted to assess evidence of group differences for these baseline variables (Teare et al, 2014).

Primary objective: Feasibility and Intervention Adherence

To fulfil the study objectives outlined above, participant flow will be extracted and summarized in Figure 1. The following outcome variables will be included as they relate to feasibility and intervention adherence. Specifically, the following variables will be extracted:

Recruitment and retention rate

- Number of community partner sites referring to the study
- Number of caregivers referred by each participating site
- Number and proportion of caregivers deemed eligible out of those that initiated the enrolment/intake stage
- Number and proportion of caregivers consenting to participate out of those found eligible overall by each participating site
- Number of participants randomised overall and by trial arm
- Number of participants withdrawing overall and by trial arm

Data completeness/adequacy

- Number of participants completing the Baseline assessment
- Number of participants completing the Follow-up assessment overall and by trial arm

Intervention adherence (by trial arm):

- Number and proportion of CST arm participants attending all 9 Group Sessions, all 3 Virtual Home Visits, and all 4 Telephone Calls
- Average number and standard deviation of Group Sessions attended, Virtual Home Visits completed, and Telephone Calls completed

Secondary Objective: CST Effect Estimates

Caregiver-child outcome variables

We will estimate preliminary CST effect sizes on the following outcomes collected at Baseline and Follow-up:

- Caregiver-child interactions will be assessed by blinded raters of caregiver-child interactions using the Dyadic Communication Measure for Autism (DCMA; Hurdry, 2013). Specifically, parent Synchrony, calculated as the proportion of all Caregiver communication acts (i.e., the total number of Synchronous, Asynchronous, and Other acts) which are Synchronous, and Child Initiation, calculated as the proportion of all Child acts that are Child Initiations, will be used.
- Caregiver distress will be assessed using the Distress Thermometer as a single-item rated by the caregiver on a 10-point Likert scale from 0 (no distress) to 10 (extreme distress).
- Family empowerment will be measured using the Family Empowerment Scale, a 34-item rating scale with 3 subscales (Family, Service System, and Community). Specifically, the 12-item Family subscale total score will be used.
- Child emotional and behavioural problems will be measured using the Strengths and Difficulties Questionnaire, a 25-item scale consisting of 5 problem scales. A total difficulty score calculated from 4 out of the 5 problem scales and the total impact subscale, will be used.
- Child language will be assessed using the MacArthur Communicative Development Inventories administered in the preferred language (English or French). Specifically, the total number of words produced (Part I-A) will be used.

Data analysis will be done in Stata (Version 17.0 or higher). Distributional assumptions for regression models will be checked using visual methods (i.e. plots of residuals to check if residuals are normally distributed, scatterplots of standardised residuals to check homoscedasticity) and nonparametric approaches used where necessary.

Preliminary effect estimates for CST outcomes will be produced along with 95% CIs and p-values but treated as exploratory. Outcomes will be analysed using multivariable linear regression analysis. Continuous outcomes will be modelled using linear regression, with post-intervention score predicted by the following (fixed effects): treatment (CST or control), stratifier (French or English), and baseline measurements of continuous outcomes. Mean differences with 95% confidence intervals in continuous outcomes between trial arms will be reported. Other ad-hoc analyses may be requested by the trial clinical team.

Adverse event reporting

No information on adverse events will be collected.

Loss to follow-up and other missing data

The number and proportion withdrawing and lost to follow-up will be summarised overall and by trial arm. If reasons for withdrawal have been captured, these will be summarised overall and by trial arm. The number and proportion of participants missing each measure will be summarised overall, as well as in each arm and at each time point as appropriate.

Missing data will be assessed for randomness, and if missing values were missing completely at random, appropriate methods such as imputation using the overall sample mean will be considered. Since this is a feasibility study, we will not make inferential conclusions about differences between arms. Where appropriate, 95% CIs will be reported. P-values may be reported but will be treated as exploratory. There are no significance thresholds for secondary outcomes.

For individual scales, we will use published guidance on how to handle missing values. If such guidance is not available, scales may be pro-rated for an individual if 20% or fewer items are missing and pro-rating is appropriate. If there are more than 20% missing items, the scale score will not be calculated and will be missing.

Missing baseline data should be limited as participants are ideally not randomised before completion of pre-randomisation measures. If there are missing items at baseline for secondary outcomes, appropriate imputation methods may be applied (i.e. mean imputation; White and Thompson (2015). The research team will make every effort to minimise missing data at follow-up. If there is a considerable amount of missing values in secondary outcomes (>15% missingness), baseline predictors of missingness will be investigated. Baseline variables found to predict missingness in secondary outcomes will be included in adjusted regression models for secondary outcomes to make the missing at random assumption more plausible.

References

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