

Tele-rehabilitation Program: An innovative and sustainable Early Intervention service for children with Autism Spectrum Disorders

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Contents

Administrative information 4

Introduction 5

 Background & Rationale 5

 Objectives and Trial Design 6

Methods: Program Overview 6

 Setting 6

 Target population 6

 Inclusion criteria 6

 Exclusion criteria 7

 Program Implementation 7

 Implementation Strategies and Patient Flow 7

 Baseline Assessments 7

 Intervention: Standard Program 8

 Intervention: Telerehab Program 9

 Parent-delivered therapy (Home-based) 10

 Program Timeline 10

 Follow-up and Review (Standard Program and Telerehab Program) 10

 Midterm Progress Review: Visit 7 to Visit 11 10

 Final Reviews and Assessments: Visit 12 to 14 11

 Final Paediatrician review: Visit 15 11

 Transfer to Early Intervention Programs 11

Logic Model for Telerehab Program 12

Evaluation Framework 13

 Literature Review 13

 Evaluation Questions 13

 Effectiveness Trial 13

 Process Evaluation 13

 Cost-Effectiveness 13

 Indicators and Outcomes 14

Data Collection Plan 19

 Recruitment 19

 Pilot 19

 Sample Size Calculation 19

 Randomisation Process and Blinding 19

 Data Collection Time Points 20

 Exit Review for Early Withdrawals 20

Qualitative Data Collection.....	20
Data Analysis Plan.....	20
Qualitative Data Analysis.....	20
Protocol Deviation and Per-protocol Analysis.....	21
Quantitative Outcomes	21
Cost-Effectiveness Analysis.....	21
Methodology	21
Decision Problem.....	21
Objective.....	21
Target Population	22
Study Perspective	22
Comparator – Standard Care.....	22
Analysis Approach.....	22
Time Horizon.....	23
Univariate sensitivity analysis.....	23
Probabilistic sensitivity analysis.....	23
Direct Healthcare Costs	23
Health sector cost.....	23
Direct Non-Healthcare Costs	23
Transportation Costs	23
Caregiver and other care costs.....	23
Indirect Costs	23
Productivity Loss.....	23
Outcomes.....	24
Input Data for Outcomes and Cost Data for the Model	24
Data Cleaning Methodology and Approach	29
Evaluation Management	30
Evaluation Time Frame.....	30
Dissemination of Findings.....	33
Quality Assurance and Ethics.....	33
Quality Review.....	33
Research Ethics.....	33
References	34

Administrative information

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Tele-rehabilitation Program: An innovative and sustainable Early Intervention service for children with Autism Spectrum Disorders

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3. Protocol version: 8

4. Funding:

MOH HSDP project to fund manpower, material costs, training and operational costs.

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5c. Role of study sponsor and funders

5d. Composition, roles, and responsibilities of the program evaluator

Introduction

Background & Rationale

This proposal supports the evaluation of a pilot project focusing on a telerehabilitation (telerehab) model for early intervention (EI) in children with Autism Spectrum Disorder (ASD) to improve access to services and facilitate intervention in the natural environment of children and their families.

In Singapore, ASD is *ranked number one in disease burden for children 0-14 years of age*. The Child Development Unit at the National University Hospital serves 3000 children annually, of which 25-30% of children have been diagnosed with ASD. Therapists provide interim therapy for these children before entry into a community-based Early Intervention Programme for Infants and Children (EIPIC). EIPICs currently have waiting times of 6-9 months. Current limitations with our interim care includes long wait times, high cost for families, lack of manpower and space to serve the patients, poor parental involvement due to their work commitments, parental difficulties attending frequent, but necessary, in-hospital therapy and difficulty generalizing patient treatment to the home/community setting, thereby decreasing treatment effectiveness.

The proposed telerehab initiative involves the use of video conferencing technology to help address the aforementioned deficits. Offering therapy through telerehab will allow us previously unattainable benefits such as seeing the child in their home environment, allowing multiple caregivers to have access to the therapeutic training, more frequent contact with families and the ability to trouble shoot real life difficulties in real time. The important advantages to the caregivers include less financial burden arising from time off from work and travel, more access to treatment over a longer period of time and ability to access a multidisciplinary team frequently. An additional benefit for the children is they need not travel to unfamiliar environments, which is frequently distressing for children with ASD. Lastly, telerehab is a sustainable initiative allowing for less manpower to cover the growing number of patients, and the possibility to be implemented in other government run hospitals and clinics facing similar challenges.

Key benefits of this program are:

1) Enabling parent and caregiver empowerment. Early Intervention in the current model has been predominantly centre-based with initiatives to increase caregiver education. A large body of literature suggests that early intervention is highly successful when provided at the age of diagnosis, with younger children yielding better outcomes. Caregiver involvement is vital to long-term success, as they spend a significant amount of time with their child; they can support the generalizations of new skills. The National Research Council identifies parent training to be the *key component for successful intervention* for children with autism (NRC 2001), improving quality of life by reducing parental stress and increasing optimism.

2) Addressing nationally identified gaps. The Enabling Master Plan recommendations for 2012-2016 (under Ministry of Family and Social Development) identifies gaps in family involvement and support in acquiring necessary skills and knowledge to be competent in helping their children make developmental gains. CDU envisions that telerehab is a viable avenue for supporting parents in learning EI skills.

3) Improving existing parent training programmes. CDU has successfully piloted a parent-training program for children with ASD called SPEECCH. In our study of the impact of this parent-training program (2011), children made measurable progress in all four skill areas assessed ($p < 0.001$). Focus on achievable and observable family-centred developmental goals showed evidence for increased parental understanding of children's learning and behaviour & effective use of strategies for facilitating

communication and interactions to support their child's development ($p < 0.001$). However, this intervention service could not be sustained due to high caseload demands and insufficient manpower. Parent interviews during review visits identified having sustained contact with therapists and parent coaching to be key areas of need.

Currently the service provides intervention for 24 children with ASD weekly for one hour across 12 weeks, and continued support for up to 20 weeks (maximum of 16 hours of intervention). Of the new referrals of 300 children with ASD, if a sustained service is to be provided, only 50% of children will receive intervention. In order to address the demand, the frequency and intensity of intervention has had to be sacrificed to be able to provide some service to all patients. *Hence to maximize the impact of early intervention, a sustainable model of service delivery using technology through video conferencing is being proposed.*

Objectives and Trial Design

We propose to evaluate the implementation and effectiveness of delivering telerehabilitation using a randomised, controlled, parallel group non-inferiority trial, supplemented by qualitative analysis. Participants willing to participate in the proposed research study and providing informed consent will be randomized to either the experimental (telerehab program) or control (standard program) arm of the intervention. In addition, we will evaluate the service model objectives of increased efficiency and sustainability, compared to current standard of care (clinic-based delivery).

Methods: Program Overview

Setting

Child Development Unit, NUH

Target population

The target population for the program consists of children referred to the Child development Unit at National University Hospital, a tertiary care hospital. Children in the target population meeting all the inclusion criteria will be eligible to enrol in the evaluation study. They will be excluded if they meet any of the exclusion criteria. We will not be advertising this study to the public.

Recruitment: Children found to be at risk for Autism Spectrum Disorders (ASD) on clinical evaluation by Developmental Paediatrician based on Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) criteria will be considered for the study. DSM-5 is the handbook used by healthcare professionals as the guide to the diagnosis of mental disorders including ASD.

Inclusion criteria

1. Children aged 15-48 months
2. Children meet cut off score for Autism Spectrum Disorders (ASD) on Autism Diagnostic Observation Schedule-2 (ADOS): The Autism Diagnostic Observation Schedule (ADOS) is a semi-structured assessment of communication, social interaction, and play (or imaginative use of materials) for individuals suspected of having autism or other pervasive developmental disorders. The ADOS consists of a toddler module and four other modules, each of which is appropriate for children and adults of differing developmental and language levels, ranging from nonverbal to verbally-fluent. The ADOS consists of standardized activities that allow the examiner to observe the occurrence or non-occurrence of behaviours that have been identified as important to the diagnosis of autism and other pervasive developmental disorders across developmental levels and chronological ages.
3. Parent(s) is/are willing and able to give informed consent

4. Families with at least one parent who is digitally literate with the home use of the internet and access to Wi-Fi
5. The same parent(s) or caregiver(s) in attendance for most intervention sessions and all review sessions in order to monitor performance across outcome measures

Exclusion criteria

1. Participants not having access to the internet will be excluded
2. Received or receiving other treatment or interventions (*Note: this is an exclusion criterion but not a withdrawal criterion*)
3. Children with genetic and other associated auditory or visual impairment and/or seizure disorders

Program Implementation

The current standard program for early intervention treatment is in-clinic therapy based on the **Foundational Skills Curriculum (FSC)**: a framework for early intervention developed from outcomes of an Autism research project conducted in the UK. This framework provides a clear and systematic approach to understanding the child's functioning in 3 core areas of development (across 141 items): Play, Social Interaction, and Communication.

The telerehab program will provide parent coaching on EI through video conferencing using the FSC. The telerehab program aims to improve access to services and facilitate intervention in the natural environment of children and their families by developing video conferencing (VC) as a feasible and acceptable medium to build parent capabilities in EI. The specific service model objectives are to realize positive gains in service efficiency (i.e. reducing the total time and resource utilization per completed intervention course relative to current practice); reduce total costs and non-financial barriers for patients (i.e. access) as well as the total cost to the health system per completed course (i.e. sustainability) and realize positive gains in provider productivity and hence cost-effectiveness (i.e. reduced cost per unit outcome achieved).

Implementation Strategies and Patient Flow

CDU receives referrals from polyclinics for children at risk of ASD. These referrals will be scheduled for a developmental assessment by the developmental paediatrician. Baseline assessments will be conducted under the program as well as under standard care. Children who are enrolled into the evaluation study will then continue with either the standard program (clinic-based therapy) or the telerehab program. The program schedule for the patient in terms of type of visits and intervention blocks for both the standard program and telerehab is shown in Annex 1: Program Schedule. The duration of clinic-based intervention sessions will be 60 min while the duration of VC based intervention sessions will be 45 min.¹

Baseline Assessments

Visit 0/1: Child found to be at risk for ASD on clinical evaluation by the developmental paediatrician based on the DSM-5 criteria will be referred for this study. The informed consent will be obtained prior to undergoing any research-related activities.

Visit 2 to 3: Upon parent consent in Visit 0 or 1, the child will be assessed on the MSEL and ADOS. However, MSEL assessment may be conducted before informed consent as part of clinical routine practice. They will also be assessed on the Vineland Adaptive Behaviour Scales (VABS) and

¹ Clinic-based intervention sessions are 60 minutes while VC based intervention sessions are 45 minutes. This includes an additional 15 minutes for therapists' administrative and documentation time.

Parenting Stress Index (PSI). Children who meet the criteria for Autism on the ADOS and do not have any of the exclusion criteria will be offered to be part of the study.

Visit 4: On completion of the above assessments, the paediatrician will share the MSEL and ADOS report with parents and confirm enrolment into the study if the child meets the inclusion criteria. If the child does not, they will be referred to standard care outside the study. Children whose parents consent to be on the study will be randomly assigned to either the telerehab program (experimental arm) or standard program (control arm) using block randomisation. The paediatrician will inform parents of the study arm that they are assigned to.

Visit 5a: Initial assessments based on the FSC, Joint Engagement Rating Inventory (JERI), child's routines (parent interview) and Family Early Intervention Quality of life (FEIQoL) will be completed for all. Parents will also participate in a short demographic and cost survey. If parents are unable to complete the surveys during their clinic-based session, they will be sent the surveys through email or asked to answer the questions over a phone call. Parents may also be invited to participate in an (semi structured, in-depth) interview for evaluating the perceived effectiveness of standard care.

Visit 5b: For the telerehab group, initial assessments and observations will be collected through 2 settings, one clinic-based, as well as one using VC. The latter is done in order to observe parent-child interactions and skills demonstrated by the child in the context of the natural home environment. The VC assessment and intervention will be conducted using a MOHH commissioned VC platform. This platform will allow the therapist and parents to see, hear, and communicate with one another live in real-time. The therapist will access the program from an office computer with a web-camera in the clinic, whereas parents will access the program from their home. Parents who do not have the necessary equipment for VC will be provided with notebook computers and needed accessories. An orientation to the use and care of VC equipment will be provided.

Visit 6: Parents of children in both programs will attend a parent education workshop. The workshop will discuss the role of parents and therapists in early intervention, the key areas that children have difficulties with during development, the use of routines to facilitate the child's learning and strategies that can be embedded in routines. If parents choose to not attend the workshop or are unable to attend their scheduled workshop, parents can still proceed with the intervention phase. Parents who are unable to attend the workshop will be reminded to reschedule the workshop to the next available date and will have training slides and materials sent to them through email for their reading. Parents will have also have opportunities to seek further clarification during subsequent visits with their therapist.

Intervention: Standard Program

The profile of the child in terms of their developmental status based on initial evaluation results and an individualised intervention plan (IIP) will be discussed by the therapist with parents. The therapist will coach parents in the context of clinic-based play activities and help parents identify contexts and activities at home where the parents could follow up on the program at home. Children and their parents will receive the standard program which consists of 16 clinic-based intervention sessions of 60 min each, separated into 3 intervention blocks, with breaks in between so that parents will have opportunities to practise at home. This arrangement also allows parents who had missed their scheduled sessions to have make-up sessions during the breaks. Intervention sessions empower and equip parents with skills and strategies to engage with their child at home. Since the program involves behavioural intervention and parent coaching, active participation of parent and child are key to each session. However, realistic challenges in terms of child/parent or therapist being unwell, or when the

parent has work related commitments, may require rescheduling or cancellation of some visits. These are not anticipated to have any adverse impact on the child's health or the study.

Intervention: Telerehab Program

The intervention will commence with 2 clinic-based intervention sessions of 60 min each to provide adequate opportunity to engage in relational family-centred practices, joint decision and planning of the IIP based on initial evaluations and explore effective strategies as foundation to the subsequent interactions and coaching through VC.

Setting: Prior to intervention sessions, the therapist and parent will discuss and identify a suitable and feasible location to place the devices of their choice that would provide clear unobstructed views of parent-child interactions and activities. For 16 sessions, the therapist and parent will log onto the MOHH VC portal for the VC call.

VC sessions are provided remotely by the child's therapist from the clinic. Parents who do not have the necessary equipment for VC will be provided notebook computers and omnidirectional microphones. The MOHH commissioned VC platform will be used for observing the home session and coaching parents. Parents will orient the computer's web cam to the selected activity area in the home while using the wireless headset for communication. An omnidirectional portable microphone will be placed in the vicinity of the routine home activity so that the therapist can look, listen and understand the dynamics of parent child interactions clearly during a given daily routine involving the child.

Telerehab sessions will follow the ethical and practice guidelines of computer-mediated intervention including online communication, consent, confidentiality & privacy and security issues, verbal and nonverbal feedback.

Strategies: Parents will be trained in using evidence-based strategies (e.g., follow your child's lead, imitation & modelling, communicative temptations, playful obstructions) during playtime activities and daily routine.

Approach: Intervention sessions will be provided by therapists trained in the FSC and the parent coaching protocol. Parent-child interactions during activities at home will be observed through the VC platform commissioned by MOHH. Parents will be encouraged to interact with their child using strategies aimed at increasing their child's attention and motivation, turn-taking routines, initiating and responding to joint attention, communication, etc. Sessions will follow the collaborative practice protocol. The protocol provides an outline for the session structure (i.e. checking in, reviewing, observation, reflection, explanation and coaching of new topics and strategies, setting goals and follow-up planning in the home context and closing).

At the start of the session, the parents' progress from the past topic and any other updates will be reviewed and discussed for 5–10 minutes. This is then followed by a 10-minute parent-child play activity. The activity allows the therapist to observe the parent's competency in implementing intervention (i.e. the goals and effective use of strategies) from the previous session's coaching. Based on observations made, the therapist will coach further to strengthen parent's confidence and competency in using strategies to facilitate the attainment of specific learning objectives in the IIP. During the final 10–15 minutes of each session, the therapist will seek feedback from the parent to understand parent's clarity, comfort and confidence in implementing the intervention plan and provide further input and information if required. The therapist will also address any challenges faced or anticipated in the context of implementing the intervention in the home context. The therapist will discuss with parents to implement the intervention plan using at least two play or daily routines (naturally occurring opportunities) identified by the parent. Adult learning principles will be adopted by

the therapist to facilitate active participation in planning and intervention implementation. For clinic-based sessions, an additional 15 minutes is allocated to allow the child and parents to settle down and transit into and out of the therapist's room.

Data collection: For all subjects, video recordings of parent child interactions will be taken at 4 specific time points, namely Baseline, two Midterm reviews and Final review. Specific to the children in the telerehab arm, an additional video recording of parent-child interaction will be done through VC for each on-site review session, totalling 8 video recording time points throughout the program's duration. Recorded videos will be downloaded and transferred to a password encrypted hard drive authorized by the institution data protection and security teams. These recordings can only be accessed by authorized team members with institutional accounts and external raters. They will be used for evaluation on the JERI, NDBI-Fi and for inter-rater reliability assessment.

Parent-delivered therapy (Home-based)

At the end of each intervention session and at the end of each intervention block, a joint discussion will be held to craft a plan for parents to implement. This will include the functional goals to be embedded, specific strategies to be used that the parent has been coached in and the home routines that the parent plans to implement. Intervention related resources such as description of strategies and examples of embedding within routines and documents on the plan will be shared with parents for their reference.

Program Timeline

While set timeframes for assessments, intervention and reviews are important, this study will be implemented under routine operational conditions of the clinical service. The standard practice of having the same therapist for each session for continuity will be adopted. Scheduling challenges are an unavoidable field condition. This is compounded by the need for rescheduling of sessions at times, such as when a child/family member or therapist is unwell. For these reasons, the duration of time to complete each intervention block may vary slightly for each child. It may also vary between the intervention and control groups.

In general, where delays from scheduling occur, each child will move to the next phase of the study (i.e. intervention and follow-up reviews) only when they have completed all planned sessions in the previous phase (e.g., intervention will only begin after all baseline assessments have been completed). These are recognised as limitations of the study design and will be considered when interpreting the study findings.

Follow-up and Review (Standard Program and Telerehab Program)

Midterm Progress Review: Visit 7 to Visit 11

Paediatrician Review (two visits): The paediatrician will review the child's general developmental profile, progress and child and family needs. The clinician will make appropriate recommendations and referrals as needed.

Therapist Review (two visits): Therapists will review the child's developmental profile on the FSC and JERI to track progress on the intervention plan and for program evaluation purposes. A cost survey will also be conducted with parents during these reviews by a member of the study team to identify any changes to household income and cost burden. If parents are unable to complete the survey during their session, they will be sent the survey through email or asked to answer the questions over a phone call.

Midpoint IIP review: Therapists will review the child on the individualized intervention plan (IIP) developed after baseline assessment and plan for further intervention.

Final Reviews and Assessments: Visit 12 to 14

The final reviews and assessments will be conducted across three sessions, which can take place in any order depending on the participant's availability and therapist's schedule.

Final Review with Therapist: The child will be evaluated on the baseline assessment measures. Parents will also be given a parent satisfaction survey, cost survey and FEIQoL survey to complete. If parents are unable to complete the surveys during their clinic-based session, they will be sent the surveys through email or asked to answer the questions over a phone call. For children in the telerehab group, there will be a VC review in addition to the clinic-based assessment.

Nurse Assessment: The child will be evaluated on MSEL. The Parental Stress Index will be administered as part of this assessment.

Psychologist Assessment: VABS-III will be administered to the parent for this assessment.

Final Paediatrician review: Visit 15

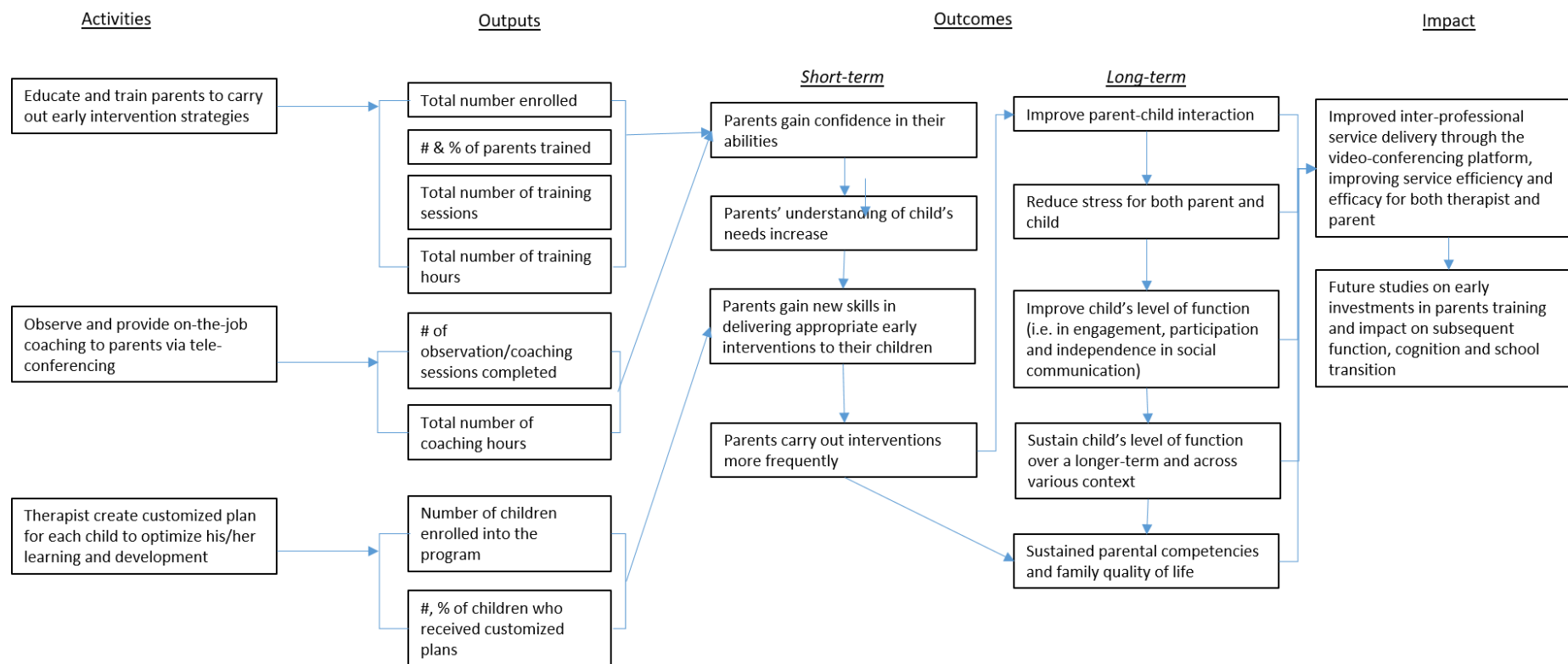
This last paediatrician visit is for the paediatrician to share the reports on the evaluations, discuss progress and further needs of child and family.

Transfer to Early Intervention Programs

CDU provides interim therapy for children pending their enrolment into an EIPIC (or private early intervention service). Under normal circumstances, the child does not receive any intervention from EIPIC in the first 10 weeks on enrolment as the child is being assessed. In this transition period, the child continues to receive CDU intervention per standard clinical practice. As such, children in this study will continue to receive intervention for 10 weeks after EIPIC enrolment. Similarly, children who has been transferred to a private intervention service will continue to receive intervention per the study protocol as long as they have not started receiving intervention at the private service.

Children also continue to remain as CDU patients under the care of their doctors until age 7, regardless of whether they have been enrolled to an EIPIC or private service. As such, study participants who have been transferred to an EIPIC will still be assessed per protocol for Midterm Progress Reviews and Final Reviews and Assessments. As far as possible, these assessments will be scheduled to coincide with their doctor's follow-up at the CDU as part of standard care.

Logic Model for Telerehab Program



Evaluation Framework

Literature Review

There is a dearth of published research on the use of telehealth in coaching for parents of children with autism spectrum disorders. A literature search found only two representative studies (Vismara et al, 2013 and Maedan et al, 2016) both from the United States and with small sample size.

One study followed eight families over a 12-week online video conference based intervention with three month follow up. Parents reported a better understanding of and appreciation for helping their children new skills, as well as increased confidence in addressing their child's needs and sharing information with other caretakers. The other described a similar Internet-Based Parent-Implemented Communication Strategies (i-PiCS) parental coaching program with 3 mother-child dyads and found positive changes in children's communication skills with the implementation of the strategies taught in coaching. As illustrated by the sample size <10 in each, neither previous study followed a rigorous RCT methodology but both studies highlighted the potential of telehealth as a feasible service-delivery option for parental coaching and called for further more robust studies of telehealth interventions with a greater diversity of participants.

Evaluation Questions

Effectiveness Trial

Primary Research Question: Is the tele-health intervention as effective as standard care in improving short and long-term outcomes for children and parents?

Process Evaluation

- How feasible and acceptable is the tele-health intervention?
- What features or conditions make the tele-health intervention more or less effective?
- What could be improved with acceptability, feasibility and scalability in mind?

Cost-Effectiveness

Is the tele-health intervention cost-effective (cost-saving) relative to standard care?

Indicators and Outcomes

Evaluation Question	Primary indicator required	Measurement & Reference	Expected change
<p>a. Is the intervention as effective as the standard care model in improving the level of function among children with ASD?</p>	<p>Mullen's Scale of Early Learning (MSEL)</p>	<p>MSEL is a standardized developmental assessment to examine developmental skills of children aged birth to 68 months on gross motor and cognitive scales using 5 subscales: Gross Motor, Visual Reception, Fine Motor, Expressive Language, and Receptive Language. T scores, percentile ranks, and age equivalents can be computed for the five scales separately.</p> <p>For each scale, the assessment derives a T-score with a mean of 50 and standard deviation of 10, a percentile score, and an age equivalent indicating at what developmental age the child is performing. An early learning composite (ELC) score is calculated from the total of scores on all scales (excepting the gross motor scale) with a mean of 100 and standard deviation of 15. T scores for subscales have a mean of 50 (SD: 10). (Bacon et al,2014)</p> <p>For children suspected of ASD, MSEL is often chosen because of its wide age range and 5 subscales that allow separate assessment of verbal and non-verbal abilities.</p> <p>Previous studies of intervention efficacy has used MSEL subscale scores for greater granularity of analysis, to understand the impact of intervention on specific functions of the child and separate assessment of verbal and non-verbal activities (Vismara et al, 2009).</p>	<p>Differences in scores on the subscales of the MSEL from baseline to program conclusion will be calculated and compared between the two intervention groups</p>
	<p>Vineland Adaptive Behaviour Scales (VABS-III)</p>	<p>VABS-III is a standardised assessment tool that utilises a semi-structured interview format to measure adaptive behavior. The main domains are: Communication, Daily Living Skills and Socialization. The Vineland-III is used for measuring an individual's daily functioning, progress planning and monitoring.</p>	<p>Differences in scores on VABS-III in communication, socialisation and daily living from baseline to program conclusion will</p>

		VABS-III provides a measure of adaptive skills used to cope with challenges of daily living. A caregiver completes a questionnaire regarding the individual's current level of functioning across three domains: communication, daily living skills and socialization. The Vineland Scales are applicable to children with and without delays from birth to 18 years, 11 months. All scales use standard scores with a mean of 100 and a standard deviation of 15, a percentile score, and an age equivalent indicating at what developmental age the individual is performing. Scores on the three domains are combined to obtain an overall adaptive behavior composite (ABC) with a mean of 100 and a standard deviation of 15.	be calculated and compared between the two intervention groups
b. Is the tele-health intervention as effective as standard care in improving parent-child interaction?	Joint Engagement Rating Inventory (JERI)	<p>JERI measures:</p> <ul style="list-style-type: none"> - joint engagement, - communication dynamics and - shared topics in a caregiver-child interaction on a 7-point likert scale (Adamson & Bakeman, 2012). <p>This is a structured assessment of joint attention and communication. It measures multiple aspects of caregiver-child interactions and identifies the specific triadic elements in engagement which are effected in Autism. This has the advantage of being a standardized assessment of social communication. It provides an insight into the dynamics of caregiver child interactions which will help in intervention planning to enhance the quality of caregiver-child engagement.</p>	<p>Change on the JERI will be tracked by calculating the changes in:</p> <ul style="list-style-type: none"> - nature of joint engagement, - child's participation in joint engagement with caregiver, - caregiver behaviours during engagement and - the range and quality of the caregiver-child interactions <p>from baseline to program conclusion and compared between the two intervention groups</p>
c.	Parenting Stress Index-	PSI-SF (Abidin, 1995) is an abbreviated version of the PSI. It is a 36-item self-report questionnaire assessing the level of relative stress in a parent-child	Change on the PSI-SF across 3 domains:

<p>Is the tele-health intervention as effective as standard care in improving parental stress?</p>	<p>Short Form (PSI-SF)</p>	<p>relationship. The questionnaire is meant for parents of young children, and can be used for the parents of children 0-12 years of age. Each item requires the parent/caregiver to rate the degree to which s/he agrees with a statement on a five-point Likert scale (1 = Strongly Agree, 2 = Agree, 3 = Not Sure, 4 = Disagree, and 5 = Strongly Disagree). The questionnaire's 36 items are divided into three subscales: Parental Distress (PD), Parent-Child Dysfunctional Interaction (P-CDI), and Difficult Child (DC). Items are scored and added together to establish a total score as well as three subscale scores.</p> <p>The PSI-SF produces subscale raw scores ranging from 12 to 60 and an overall Parenting Stress (PSI-PS) total score that ranges from 36 to 180; a higher score indicates a greater level of stress. A PSI-PS score above 85 (at the 90th percentile) indicates clinically significant parenting stress (Abidin, 1995).</p>	<p>parental distress, parent-child dysfunctional interaction and difficult child will be tracked by calculating the change in raw scores on the PSI-SF from baseline to program conclusion and compared between the two intervention groups</p>
<p>d. Is the tele-health intervention as effective as standard care at improving child outcomes over the long term and various contexts?</p>	<p>Mullen's Scale of Early learning (MSEL) Early learning Composite (ELC)</p>	<p>For each scale, the assessment derives a T-score with a mean of 50 and standard deviation of 10, a percentile score, and an age equivalent indicating at what developmental age the child is performing. An early learning composite (ELC) score is calculated from the total of scores on all scales (excluding the gross motor scale) with a mean of 100 and standard deviation of 15. T scores for subscales have a mean of 50 (SD: 10) (Bacon <i>et al.</i>, 2014).</p> <p>Early learning composite score has also been widely used as a score to compare effectiveness of early intervention programs (Shank 2011, Bishop <i>et al.</i>, 2011).</p>	<p>Differences in ELC score from baseline to program conclusion will be calculated and compared between intervention groups</p>
<p>e. Is the tele-health intervention as acceptable as standard care?</p>	<p>Parent Satisfaction Survey and Parent Interview</p>	<p>Parent Satisfaction Survey: This 13-item survey uses a 5-point Likert scale to obtain parents' feedback on the telerehab program at the end of the intervention. Each item requires the parent/caregiver to rate the degree to which s/he agrees with a statement on a five-point Likert scale (1 = Strongly Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, and 5 = Strongly Agree).</p>	<p>Parent Satisfaction Survey will be collected at the end of the study and the responses will be compared between the two intervention groups</p>

		<p>Pre-Programme Parent Interview on the following prior to parents starting on telehealth intervention program:</p> <ol style="list-style-type: none"> 1. Demographics 2. Current situation (Knowledge, Existing sources of support and coping mechanisms, perceived barriers) 3. Telehealth Programme Intervention (Technology comfort, motivation, expectations, perceived barriers/challenges) <p>Post-Programme Parent Interview on their experience with the telehealth intervention program.</p> <p>Interviews will only be conducted with participants who have indicated interest and consented to participate in the qualitative interviews.</p>	
<p>f. Is the tele-health Intervention as effective as standard care in enhancing the family's perceived quality of life?</p>	<p>Families in Early Intervention Quality of Life (FEIQoL)</p>	<p>FEIQoL includes 40 items across 4 areas rated on a 5 point Likert scale:</p> <ol style="list-style-type: none"> 1. Family Relationships (Problem solving, communication, parenting, relationships with extended family, and family participation in social activities) 2. Access to Information and Services Knowledge of their child's disability, child development, managing challenging behaviors and resources such as support services, medical assistance, and organizations in their community 3. Child Functioning (Child's engagement, independence, and social relationships within family daily routines) 4. Overall Life Situation (Fulfillment of family needs in health, financial resources, and employment.) 	<p>Change on the FEIQoL will be tracked by calculating the changes on the 4 areas from baseline to program conclusion and compared between the two intervention groups</p>
<p>g. Is the tele-health intervention more cost-effective than</p>	<p>Total direct and indirect costs from health system and societal perspective</p>	<p>Total direct and indirect costs from health system perspective: Total intervention costs, including development costs, cost of using the videoconference platform, labour and infrastructure as well as total medical costs and costs of other interventions incurred by parents as related to ASD. Costs related to the evaluation alone will be excluded.</p>	<p>Compare total direct and indirect costs from baseline to program conclusion from health system and societal</p>

the standard care?		Total direct and indirect costs from societal perspective: As above and also including cost of travel and productivity losses incurred by parents.	perspective between two intervention groups
h. Is the tele-health intervention effective in improving parents' implementation of intervention strategies?	NDBI (Naturalistic Developmental Behavioural Interventions)-Fi	NDBI-Fi is an 8-item observational rating scheme that evaluates caregiver implementation of common strategies from treatments classified as NDBI based on short videos of caregiver-child interactions.	Change on the NDBI-Fi will be calculated by tracking the changes on individual items and average rating from baseline to program conclusion for participants in the telerehab arm

Quantitative process indicators (the outputs indicated in the logic model) will be assessed in the intervention group as well as part of monitoring and process evaluation.

The qualitative research questions will enhance our understanding of both the impact and process-related outcomes, using semi-structured interview guides. Parents will be asked about perceived effectiveness, engagement and stress, as well as their ability to cope financially with treatment. At baseline, we will also investigate attitudes/perceptions towards telerehab, and factors that affect willingness to take up telerehab. At the end of the study, while the scope of the quantitative evaluation is limited, we will explore parent experiences, satisfaction and concerns, and perceptions of sustainability and future care plans.

Data Collection Plan

Recruitment

Patients will be recruited for the program after obtaining a preliminary diagnosis of ASD from the developmental paediatrician. ADOS-2 will be administered to confirm the diagnosis and thus participation in the research study. We will not be advertising this study to the public.

Pilot

An initial pilot feasibility study with 6 children and families will be conducted at the start of the project to identify any practical issues or weaknesses in the program or protocol before full scale evaluation.

Sample Size Calculation

The randomized trial is designed as a non-inferiority study to compare the changes in MSEL between 2 interventions. We expect that the change in MSEL score for the subjects in the new intervention arm will be slightly better than that in the control arm by 1.5 units. Assuming the SD of changes in MSEL score is 15 units, with 5 units as the non-inferiority margin, based on a one-sided test with 80% power and 5% significance level, it is sufficient to recruit 132 subjects (66 in each arm). We decided to recruit 200 subjects in total (100 in each arm) after considering withdrawals and lost to follow up. The computation was performed using a proprietary software programmed in R.

Randomisation Process and Blinding

Computer-generated randomisation will be used to randomly assign the participants to one of the intervention groups. Block randomisation will be used to allocate the recruited subjects into one of the interventions. A randomisation list will be generated by the study statistician and envelopes will be prepared. Although the allocation of intervention will be concealed and the study team will not know in advance which subject will receive which intervention, the blinding will not be possible once the intervention is assigned. Assessors of the initial and final MSEL were not told of the intervention status of the patient to avoid bias in outcome assessment. Blinding of the parents is not possible in the context of this study. Phone calls will be made if necessary to confirm appointments and/or before commencing consultation over video conference in the Telerehab group. Parents in both study arms will be encouraged to spend 2h per week in quality interactions with their children.

Children who meet the inclusionary criteria will be randomly assigned to the standard or telerehab group of the study. Parents will be informed of the randomisation assignment and clinical diagnostic impression on ADOS. Baseline evaluation measures – Mullen's Scales of Early Learning (MSEL), Vineland Adaptive Behaviour Scales (VABS-III), Parenting Stress

Index (PSI-SF), Joint Engagement Rating Inventory (JERI) and FEIQoL (Families in Early Intervention Quality of Life) - will be completed for all.

Data Collection Time Points

The child and parents' skills will be recorded at 4 data points (baseline; 2 midterm reviews; final review) and progress tracked on the IIP, JERI and FSC. Parent questionnaires will be given at the end of the intervention to evaluate parents' experience with the technology used in the sessions, using a Likert Scale, and to evaluate their experience as *providers* of intervention services to their child. Video analyses will be performed by external raters. Inter-rater reliability will be calculated based on the assessments of raters (number of agreements/number of agreements plus disagreements). Hospital resource use pertaining to the intervention will be recorded at each point as well as healthcare expenditures and household resource use, travel expenses and caregiver time spent.

All clinical data will be collected in the case record form designed for the collection of data for the study. For the various assessment tools that will be used, data will be collected on the assessment tool itself, which will serve as the source of that data.

All data will be later transcribed to excel sheets or other relevant databases as soft data for statistical analysis. The data will be coded to remove any patient identifiers before sharing with the statistician for analysis.

Exit Review for Early Withdrawals

If the participant has completed their first block of intervention and requests to withdraw from the study before their final reviews and assessments (Visit 12 to 14), they will be presented with the option to come back to the clinic for an exit review before withdrawing. In the exit review, the child will be assessed on MSEL, parental stress index, parent satisfaction survey, cost survey, FEIQoL and VABS. Specific to the children in the telerehab arm, an additional video recording of parent-child interaction will be done through VC. However, participants can opt to not come back for the exit review and withdraw from the study immediately.

Qualitative Data Collection

In-depth interviews (IDIs) would be conducted twice: (i) before parents participate in the program and (ii) at the end of the program or before they withdraw from the program or when they are transiting out of the program to receive early intervention beyond CDU before the completion of the program.

Recruitment strategy: To space the recruitment of participants for IDI, we will recruit every 3rd participant (caregiver of patient) enrolled into the study, have consented to participate in the IDI and will be able to undergo the interview in English. We estimate that we will recruit up to 10 parents in each study arm (standard and telerehab group) i.e. 20 parents, 2 interviews each and 40 interviews in total.

Data Analysis Plan

Qualitative Data Analysis

For the qualitative research component, applied thematic analysis would be used to analyse the qualitative data gathered to understand the concerns and experience of the programme from the perspectives of the parents.

A professional transcriptionist will complete data transcription. A standard operating guideline and format of the verbatim will be established jointly by the principal researcher and the transcriptionist. Subsequently, the qualitative analysis research team will perform an iterative and inductive process of identifying new themes and sub-themes derived from participants' narratives. A codebook that best describe the data would be developed and used through coding and constant comparison to establish inter-coder reliability by the team for the analysis of all transcripts.

Protocol Deviation and Per-protocol Analysis

Protocol deviation is defined as any divergence from what was pre-planned and approved by the institutional review board. As the study is conducted as part of routine care and operations, there are practical constraints that may cause protocol deviations to occur. Rescheduling of appointments by the parents (e.g. due to work constraints, child's sickness, other events) or defaulting appointments is inevitable. Hence, for per-protocol analyses, we will only exclude participants with major protocol deviation, which will be defined as participants who do not complete 80% of the intended therapy sessions allocated for their study arm. This means that a control arm participant must attend at least 8 out of 10 clinic-based sessions. For the remaining 2 sessions, participants can either be attending it through video-conferencing (due to the COVID-19 pandemic) or miss the appointment.

Quantitative Outcomes

For the randomized trial, since the study is a non-inferiority study, statistical analysis will be carried out on a per-protocol basis. Subjects with any major protocol deviation as defined above will be excluded from the final analysis.

All demographic, clinical and cost characteristics will be analysed descriptively. Mean (SD) or median (range), whichever is more appropriate will be reported for numerical variables, while N (%) will be reported for categorical variables. 2-sample t-tests, or Mann-Whitney U tests will be used to compare the change of MSEL score between 2 arms. Mean difference and 95% CI will be estimated. If the lower boundary of the 95% CI is more than -5, non-inferiority will be declared. Changes in the quality of parent-child engagement, parental stress index score, and adaptive score will be compared by using either a 2-sample t-test, or a Mann-Whitney U test, whichever is more appropriate. Linear regression will be used to adjust for any covariates.

Cost-Effectiveness Analysis

To examine cost-effectiveness, we will compare resource utilization between treatment and control groups to estimate resource and cost differences in absolute terms from the direct medical cost perspective as well as the societal perspective (inclusive of the direct costs of travel and the indirect cost of parental time). As the trial focuses on non-inferiority, the assessment of cost-effectiveness will rely on whether the intervention is cost-saving relative to the standard of care. We will also perform modelling estimates to quantify the uncertainty surrounding the incremental cost-effectiveness ratio.

Methodology

Decision Problem

Objective

To assess the cost-effectiveness, in terms of incremental cost effectiveness ratio (ICER) of the **tele-health (telerehab) mode** of delivering the early intervention (EI) in children with

Autism Spectrum Disorder (ASD) relative to the **standard care** (clinic-based sessions only) in costs and outcomes as measured by Mullen Scales of Early Learning (MSEL), Vineland Adaptive Behavioural Composite score (VABS) and Joint Engagement Rating Inventory (JERI).

$$ICER = \frac{Costs_{New} - Costs_{Old}}{Effects_{New} - Effects_{Old}}$$

Figure 1: Incremental cost-effectiveness ratio (ICER), calculated by the difference in cost between two possible interventions, divided by the difference in their effect.

Target Population

The study target population for these analyses will be the children assessed to fulfil the inclusion criteria of the Telerehab RCT from NUH CDU. The delivery of early intervention heavily involves a caregiver, often the biological parent(s) of the children receiving therapy for early intervention.

Study Perspective

The study will take on a **societal perspective**. This includes healthcare costs from the provider’s perspective, non-healthcare costs incurred by the patient from social care and child care, as well as productivity losses for the patient’s caregiver.

The time horizon of the study includes the cost incurred and benefits from the entire program duration, from enrolment to the final review.

Comparator – Standard Care

The comparator for this study will be the standard model of delivery for EI which are clinic-based (face-to-face) sessions with the patients and their primary caregiver. The **variable treatment component** between telerehab and the standard model of delivery is the number of video-conferencing vs clinic-based intervention sessions. The assumption is that all non-therapy related costs such as paediatrician reviews will be the same for subjects in both study arms.

Table 1: Variable components of care between standard and telerehab care model

	Standard Model	Telerehab Model
Clinic-based intervention (45mins + 15mins)	16 sessions	2 sessions
Video-conferencing (30mins + 15mins)	0 sessions	16 sessions
Total Therapy time	720mins + 240 mins (admin)	570mins + 270 mins (admin)

Analysis Approach

We will take on two approaches to calculate the ICER. First, is the use of patient-level data for cost-effectiveness analysis. Second, we will use estimates generated from analyses Monte Carlo simulation to estimate the cost-effectiveness through parameters (mean, standard errors) obtained from the study. This will be decided by the analyst with the justification for the approach documented.

Time Horizon

The time horizon considered will be the duration of the program (around 1 year), from enrolment till final review. The cost and outcomes data collected will be limited to the duration of the program. It will be hard to justify extrapolations and assumptions after the program after the patient has transited out of NUH CDU to EIPIC, where treatment frequency and intensity will be substantially variable.

Univariate sensitivity analysis

One-way sensitivity analysis will be performed to assess the impact of a change in parameters.

Probabilistic sensitivity analysis²

Probabilistic sensitivity analysis (PSA) will be performed by incorporating the degree of uncertainty for each parameter. This involves assigning a primary mean value for each model parameter (mean cost, number of visits, probabilities) and the distribution of possible values. Monte Carlo simulation was used to estimate mean expected costs and outcomes, and statistical measures of expected variance (SD) around the mean for 1,000 iterations drawn from the distributions defined.

Direct Healthcare Costs

Health sector cost

Health sector cost will be primarily attributed to the cost of treatment delivered by the institution, NUH CDU. The gross charges for paediatrician review, IIP review and administering surveys and assessments for the children are consistent in both study arms. Only variable cost between both study arms will be included. The variable cost includes the clinic-based intervention charges and video-conferencing-based intervention charges across both arms. The assumption for health sector cost will be that participants from both arms attend all the review and assessment sessions as they are essential to the intervention plan. The only variability would be attributed to defaulted therapy sessions.

Direct Non-Healthcare Costs

Transportation Costs

Transportation cost will be estimated using the responses from the baseline cost survey administered to caregivers. The total transport cost per study arm (standard vs telerehab) will be calculated by multiplying the *observed number of clinic-based visits* (accounting for missed appointments/therapy sessions) with the average cost of transportation indicated by the caregiver multiplied by two to account for round-trip travelling.

Caregiver and other care costs

Costs from other sectors include care cost from attending courses, hiring domestic helpers and/or other forms of care support for the child. This information is obtained from the cost survey administered to the parents.

Indirect Costs

Productivity Loss

Productivity loss will be calculated using the human capital approach. The human-capital method takes the patient's perspective (in this case the parent's time) and counts any hour not worked as an hour lost.

² <https://yhec.co.uk/glossary/probabilistic-stochastic-sensitivity-analysis/>
TRAutism HSDP Protocol_Version 8_19/08/2022

Productivity loss in this study will be primarily attributed to the caregiver taking time off from work to attend treatment with the patient (their child) and applying intervention strategies with the child. The time spent by caregivers includes the following:

- i. time spent on travelling CDU for treatment (two-way trip);
- ii. time spent on therapy sessions (30mins for video-conference, 45mins for clinic-based);
- iii. employment charges

Outcomes

We will examine the primary outcome, Mullen's Scale of Early Learning (MSEL) Early Learning Composite Score (ELC) as the key outcome of interest (i.e. the denominator for ICER). We will also examine the outcomes in VABS and JERI as outcomes of interest. Parameters for modelling for outcomes will be obtained from analyses specified in the previous section.

Input Data for Outcomes and Cost Data for the Model

The input data for the model from the survey administered is listed below in Table 2.

Table 2: Data Source and Parameters Estimates and Distribution for Cost-effectiveness Analysis

	Standard	Telerehab	Parameters Estimated	Distribution
Outcomes	Estimates from analysis from t-test/regression for: MSEL-ELC, VABS composite score and/or JERI	Estimates from analysis from t-test/regression for: MSEL-ELC, VABS composite score and/or JERI	Mean (SD) improvement in outcomes examined	Normal
Direct Healthcare Cost				
Attendance for therapy sessions	Number of clinic-based therapy sessions attended	Number of clinic-based and telerehab therapy sessions attended Telerehab consists of clinic-based sessions at the start of the program + telerehab sessions	Mean (SD) of therapy session attended across each study arm	Normal or gamma
Healthcare cost	Total cost of clinic-based therapy sessions	Total cost of clinic-based + telerehab therapy sessions	Number of visits * fixed cost per visit (standardized for FY2021/22)	Fixed
Direct Non-healthcare Cost				
Transport costs	Survey questions <ul style="list-style-type: none"> • What mode of transport did you use to get here today? • How much did it cost? • Do you usually use this mode of transport to get to the clinic/CDU? • If no, what is your usual mode of transport? • How much did it cost? 	Survey question <ul style="list-style-type: none"> • What mode of transport did you use to get here today? • How much did it cost? • Do you usually use this mode of transport to get to the clinic/CDU? • If no, what is your usual mode of transport? • How much did it cost? 	The total transportation cost incurred by participants will differ between study arms by nature of the mode of delivery. The actual transportation cost will account for two-way (round trip) and the observed visits (accounting for missed appointments for example)	Normal

			Transport Cost = Total no. of trips * Mean transport cost * 2	
Caregiver and other care cost	<ul style="list-style-type: none"> [At review] Did you pay for help (courses, caregivers, domestic helpers) after learning about your child's diagnosis? How much did you pay? 	<ul style="list-style-type: none"> [At review] Did you pay for help (courses, caregivers, domestic helpers) after learning about your child's diagnosis? How much did you pay? 	<p>Assuming that the rate of care engagement is different in both study arms, the cost of engaging additional care.</p> <p>Care cost = Probability of engaging additional care by group * mean cost care by groups</p>	<p>Probability of requiring additional care = Beta</p> <p>Cost of added care = Gamma</p>
Indirect Cost from Productivity Loss				
Baseline change in employment	<ul style="list-style-type: none"> Have you or other family members changed work hours because of your child's medical or developmental condition? 	<ul style="list-style-type: none"> Have you or other family members changed work hours because of your child's medical or developmental condition? 	<p>1 Yes, someone in the family stopped working 2 Yes, someone decreased his/her work hours 3 Yes, someone increased his/her work hours 4 No</p> <p>We can base it off some assumption Assumption: 1 = 1.0 FTE Reduction 2 = 0.5 FTE Reduction 3 = 0.5 FRE Increase</p>	
Baseline anticipated change in employment	<ul style="list-style-type: none"> [at baseline] Do you foresee the need to adjust your employment situation in light of this intervention? 	<ul style="list-style-type: none"> [at baseline] Do you foresee the need to adjust your employment situation in light of this intervention? 	<p>1 Yes, reduce number of hours at work 2 Yes, make arrangements to work remotely</p>	

			<p>3 Yes, find a different job which allows me to spend more time with my child</p> <p>4 Yes, taking unpaid leave</p> <p>5 Yes, take time off</p> <p>6 Yes, Others</p> <p>7 No</p>	
Follow-up change in employment	<ul style="list-style-type: none"> • [at review] Have there been any changes to the employment arrangement at home due to the beginning of the intervention? • What is your monthly income now? 	<ul style="list-style-type: none"> • [at review] Have there been any changes to the employment arrangement at home due to the beginning of the intervention? • What is your monthly income now? 	Same as above	
Follow-up time spent on intervention for caregivers	<ul style="list-style-type: none"> • In the past month, on average how much time (in hours) do you spend engaging (Speaking to, playing with, communicating with, doing activities) with your child per day? • In the past month, on average how much time (in hours) do you spend applying strategies learnt through the intervention with your child per day? 	<ul style="list-style-type: none"> • In the past month, on average how much time (in hours) do you spend engaging (Speaking to, playing with, communicating with, doing activities) with your child per day? • In the past month, on average how much time (in hours) do you spend applying strategies learnt through the intervention with your child per day? 	<p>Productivity loss in the time spend on delivering intervention to child</p> <p>Time (in hour) spent on engagement with child + apply strategies learnt with child * hourly income of parent surveyed</p>	

Transport	<ul style="list-style-type: none"> • [baseline] How long did it take you to get to the clinic/CDU today? • Does it normally take you this long? • If no, how long do you usually take? 	<ul style="list-style-type: none"> • [baseline] How long did it take you to get to the clinic/CDU today? • Does it normally take you this long? • If no, how long do you usually take? • [At review] How long does it take for you to set up the computer before each telerehab session? 	Productivity loss in travelling time Time (in hour) required to travel to CDU today * 2 (two-way trip) * hourly income of parent surveyed	
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Data Cleaning Methodology and Approach

The surveys administered were open ended and the quality of the data obtained is variable. The approaches and steps to standardise the cleaning of data for analysis are listed in the table below.

Data entry type	Approach	Example
Range of data indicated "3000-5000"	The average value between the maximum and the minimum data will be calculated	"3000-5000" $\rightarrow (3000+5000/2) \rightarrow 4000$ "4k to 6k" $\rightarrow (4000+6000/ 2) \rightarrow 5000$
Undefined boundaries "2000+"	The operators (~, +, ++, "plus) will be removed and the numeric value will be referenced instead	"2k+ to 3k+" $\rightarrow (2000+3000/2) \rightarrow 2500$ "7+" $\rightarrow 7$ "3k~ " $\rightarrow 3000$
Variable string responses "1hr on weekday, 5hr on weekends"	Value will be taken in reference to the question	Total time spent with child per week: "1hr on weekday, 5hr on weekends" $\rightarrow (1*5) + (5*2) = 15$ Average time spent with child each day: "1hr on weekday, 5hr on weekends" $\rightarrow [(1*5) + (5*2)]/7 = 2.14$
Missing / Not Applicable "-", "N/A", "0", "Not Applicable", "NA", "None", "Null", or "INF",	Converted to missing/empty responses	"-", "N/A", "0", "Not Applicable", "NA", "None", "Null", or "INF" \rightarrow NA
Out of range values	Values that are out of range e.g. 20-30 hours for time spent with the child daily	Replace with NA, treat as missing variable

Evaluation Management

This evaluation will be conducted by the NUS Centre for Health Services and Policy Research (CHSPR) and the research team at CDU.

Evaluation Time Frame

Table 3: Evaluation Time Frame from Protocol Version 6.0 dated December 2019

Time from project start date	Phase	Activity	Milestone
Year 1 Q1	Program preparatory phase	Manpower recruitment Clinical training in FSC	
Year 1 Q2	Program development & stabilization phase	Adapt and finalize Telerehab service model for Singapore context. Conduct feasibility study with 6 children and families	Feasibility study report and review
Year 1 Q3-Q4	Implementation	Enrolment and data collection for Year 1	
Year 2 Q3-Q4	Preliminary analysis of Year 1 data	Analysis of Year 1 data including Year 1 follow-up	Interim Report
Year 2 Q1-Q4	Implementation	Enrolment and data collection for Year 2	
Year 3 Q1-Q4	Implementation	Enrolment and data collection for Year 3	
Year 4 Q2-Q3	Final Analysis	Consolidation and analysis of final data including all follow-up data	Final Report

The expected duration of the HSDP project was 3 years, from 01 June 2018 to 31 May 2021. As of January 2021, the Principal Investigator (PI) of the study, Dr Isaac Sia has decided to extend the study to fulfil the targeted recruitment number. The study is expected to end on 31 May 2023. See Table 4 for the updated evaluation time frame.

Table 4: Updated evaluation time frame as of June 2021

	Program Year	Year 1				Year 2				Year 3				Year 4				Year 5				Year 6		
	Quarter	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1		
	('YY)	18	18	18	19	19	19	19	20	20	20	20	20	21	21	21	21	22	22	22	22	23	23	
	Month	Jun	Sep	Dec	Mar	Jun	Sep	Dec	Mar	Jun	Sep	Dec	Mar	Jun	Sep	Dec	Mar	Jun	Sep	Dec	Mar	May		
Phase	Activity																							
Program preparation	Manpower, training	X																						
Program development & stabilization	Adapt and finalise, conduct feasibility study		X																					
Implementation	Enrolment and data collection for Year 1			X	X																			
Implementation	Enrolment and data collection for Year 2					X	X	X	X															
Preliminary data analysis	Analysis of Year 1 data including Year 1 follow-up							X	X															
Implementation	Enrolment and data collection for Year 3									X	X	X	X											
Study-Progress Report	For MOH Grant Extension												X											
Implementation	Enrolment and data collection for Year 4													X	X	X	X							

MOH Bi-Annual report	Every March and Sep														X		X					
Implementation	Data collection for Year 5 (no more enrolment)																	X	X	X	X	
MOH Bi-Annual report	Every March and Sep																		X		X	
Final Analysis	Consolidation and analysis of final data																					X

Dissemination of Findings

We propose to disseminate results to three primary groups of internal and external stakeholders

Group	Aim	Timing of dissemination	Method
NUHS management	To make decisions about the program but also about the general policies related to “big data”	Ongoing	Briefing and research round presentations
HSDP management / MOH stakeholders		Periodic results per the HSDP contract.	Reports, briefing; at discretion of HSDP/MOH
Academics, researchers and clinicians	To support	After endline data collection	Publications, presentations, seminars

Quality Assurance and Ethics

Quality Review

To ensure quality for the evaluation, we will seek review of the final analysis and report by an independent senior faculty member affiliated with CHSPR.

Research Ethics

Approval will be sought from the National Healthcare Group Domain-Specific Review Board. Protocol amendments will be conveyed to the DSRB review panel for approval before changes are carried out in the trial. Any changes in documents used (e.g., informed consent form, case report forms, data collection forms) will also be sent to the DSRB for approval.

The study will be conducted in accordance with the protocol, International Conference on Harmonization (ICH) GCP guidelines, applicable regulations and guidelines governing clinical study conduct and ethical principles that have their origin in the Declaration of Helsinki. The investigator will ensure that the study is conducted in accordance with the provisions as stated in the ICH regulations and complies with prevailing local laws and customs. Prior to the initiation of any screening or study-specific procedures, the investigator and/or his/her representative will explain the nature of the study to the child's parents and answer all questions regarding this study. Each informed consent will be reviewed, signed and dated by the child's parents and the person who administered the informed consent. A copy of each informed consent will be given to the child's parents and each original will be placed in the Investigator Site Manual.

Information collected for this study will be kept confidential. Patient records, to the extent of the applicable laws and regulations, will not be made publicly available. Data collected and entered into the Case Report Forms are the property of NUH. In the event of any publication regarding this study, patient identity will remain confidential.

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Annex 1: Program schedule

Visit no.	Standard program		Telerehabilitation program	
	Test/Intervention	Time (min)	Test/Intervention	Time (min)
ASSESSMENT PHASE				
Visit 0	First Paediatrician visit Screening for ASD (DSM-5) Initiate informed consent taking for study (refer to consent form) – can be done at Visit 0 or 1			30
Visit 1	Second Paediatrician visit Initiate informed consent taking for study (refer to consent form) – can be done at Visit 0 or 1 Refer for ADOS and MSEL if consent is given Otherwise continue with standard care			30
Visit 2-3	Nurse Assessment MSEL + PSI			120
	Psychologist Assessment ADOS + VABS			120
Visit 4	Third Paediatrician visit Paediatrician visit to share Mullen's & ADOS-2 report and confirm enrolment into the study and to inform arm of study. If patient does not meet the inclusion criteria. They will be referred to standard care outside the trial.			30

Visit 5	Therapist Assessment (clinic based)			90
	<ul style="list-style-type: none"> • Foundational Skills Curriculum (FSC) assessment • Parent interview on routines • Joint engagement rating inventory (JERI) • Family Early Intervention Quality of life survey (FEIQoL) • Demographic survey • Cost Survey 			
			Preparation for video conferencing Video conferencing observation (FSC, NDBI-Fi)	30
Visit 6	Parent Education Workshop (Can be conducted either in person or through electronic training slides)			90
For eligible and chosen participants, pre-interview will be conducted between visit 5 and before the Intervention Phase.				45
INTERVENTION PHASE				
1 st block of intervention	Clinic-based intervention (CBI) x 6 (Commencement of Individualised intervention plan (IIP))	60 x 6	Clinic-based intervention (CBI) x 2 (Commencement of Individualised intervention plan (IIP))	60 x 2
			Video conference-based intervention (VCBI) x 4	45 x 4
Parent-delivered therapy home-based)				
2 nd block of intervention	Clinic-based intervention (CBI) x 4	60 x 4	Video conference-based intervention (VCBI) x 4	45 x 4

Visit 7-8	Fourth Paediatrician visit Midpoint Review by paediatrician (clinic based or teleconsultation)			30
	<ul style="list-style-type: none"> • Child's profile, progress • Child and Family's needs • Appropriate recommendations and referrals (if needed) 			
	Midterm Progress Review with Therapist (clinic based)			60
	<ul style="list-style-type: none"> • Foundational skills curriculum – Child's development profile • Joint Engagement Rating Inventory (JERI) • Cost Survey 			
Parent-delivered therapy (home-based)				
Visit 9	Midpoint IIP Review with Therapist (clinic based)	60	Midpoint IIP Review with Therapist (clinic based)	60
3 rd block of intervention	Clinic-based intervention x 6	60 x 6	Video conference-based intervention (VCBI) x 2	45 x 2
	Parent-delivered therapy (home-based)			
Visit 10-11	Fifth Paediatrician visit Midpoint Review by paediatrician (clinic based or teleconsultation)			30
	<ul style="list-style-type: none"> • Child's profile, progress • Child and Family's needs • Appropriate recommendations and referrals (if needed) 			
	Review with Therapist (clinic based)			60
	<ul style="list-style-type: none"> • Foundational skills curriculum – Child's development profile • Joint Engagement Rating Inventory (JERI) • Cost Survey 			

4 th intervention block	Parent-delivered therapy (home-based)	Video conference-based intervention (VCBI) x 6	45 x 6
		Parent-delivered therapy (home-based)	
Visit 12-14	Final Review with Therapist (clinic based)		90
	<ul style="list-style-type: none"> • Foundational skills curriculum (FSC) assessment • Joint engagement rating inventory (JERI) • Family Early Intervention Quality of life survey (FEIQoL) • Cost Survey 		
	Additional Indicators to baseline:		
	<ul style="list-style-type: none"> • Parent Satisfaction Survey 		
	Final Nurse Assessment (clinic based)		120
	<ul style="list-style-type: none"> • MSEL & PSI 		
	Final Psychologist Assessment (teleconsultation)		60
	<ul style="list-style-type: none"> • VABS-III 		
		Video conferencing observation (FSC, NDBI-Fi)	30
Visit 15	Sixth Paediatrician visit (final visit)		30
	Paediatrician to share reports and discuss progress and further needs of child and family		
Post-interview will be conducted for eligible and chosen participants after intervention is completed, or after participant has transitioned to EIPIC.			45
End of study			

Annex 2: Comparison of 2 programs (standard and telerehab)

Standard & Telerehab	
The FSC framework is drawn with specific focus on Autism needs and impairments. The core areas of Autism are subsumed in the framework.	
Curriculum framework for autism early intervention developed as an outcome of Autism research project, UK <i>FSC program Reference: From Val Cumine, Julia Dunlop and Gill Stevenson, Autism in the Early Years, 2nd ed., London: Routledge. © 2000, 2010 Val Cumine, Julia Dunlop and Gill Stevenson.</i>	
This framework has been used in CDU since 2010 and is currently referred to as “Foundational Skills Curriculum”.	
Assessment includes an observational profile under 4 key areas of need in Autism: <ol style="list-style-type: none"> 1. Social interaction (gaze, proximity, Imitation, Initiation, turn taking, Emotional expression & understanding & development of Self) 2. Communication (understanding simple verbal and non verbal approaches, Strategies for meeting needs, Engaging in social interaction, Joint attention strategies, and 3. Play skills (types of play and interaction during play) and 4. Daily routines (Independent daily living skills and participation) <p>Though Behaviour is not explicitly included in the observational profile, the book with this approach provides detailed information and guidelines for behaviour assessment and intervention.</p>	
Uses a developmental framework with specific inclusions of skill sets relevant to autism	
Intervention-guiding principles: An eclectic approach which includes principles of: <ul style="list-style-type: none"> • building relationships, • use of structured teaching, • interactive play strategies, • use of visual supports, • Functional behaviour analysis and positive behaviour support, • SCERTS model and • activity based intervention and embedding intervention into everyday routines • use of natural environment • Individualized learning plan • family partnerships • transdisciplinary practice 	
HSDP research study (control arm/standard program):	HSDP research study (experimental arm /telehealth program):

<p>FSP is implemented <u>purely as a clinic based intervention program</u> (in the current standard service)</p> <p><u>Baseline assessments:</u> Clinic based session</p> <p><u>Intervention:</u> 16 clinic based intervention sessions conducted in the context of play activities in the clinic.</p> <p><u>Approximate duration of intervention:</u> 40 to 60 weeks</p>	<p>FSP is being piloted to implement <u>as a telehealth service</u>. The proposed implementation includes:</p> <p><u>Baseline assessments:</u> Clinic based session + one observation conducted through video conferencing. (This observation will provide valuable insight into the quality of parent child interactions in a natural home context and routine.)</p> <p><u>Intervention:</u> 2 clinic based intervention sessions 16 intervention sessions will be conducted through video conferencing in the context of naturally occurring parent-child interaction in a daily routine.</p> <p><u>Approximate duration of intervention:</u> 40 to 60 weeks</p>
<p><u>Clinic based intervention format:</u></p> <ul style="list-style-type: none"> • Initial assessment • IIP planning • Group parent education workshop • Total of 3 blocks of intervention (16 sessions – 60 min / session) <p><u>Session protocol:</u> Clinic based intervention protocol:</p> <ul style="list-style-type: none"> • Observation of parent child interactions • Exploration of potentially effective strategies and contexts to embed goals • Demonstration of embedding goals and strategies • Guided feedback: caregiver practice with guidance and support from Interventionist • Reflection & problem solving of the whole exercise 	<p><u>Video conference based intervention program format:</u></p> <ul style="list-style-type: none"> • Initial assessment • IIP planning • Group parent education workshop • Total of 4 blocks of intervention (2 clinic based intervention sessions 60 min / session and 16 video conference based intervention sessions 45 min / session) <p><u>Session protocol:</u> Clinic based intervention protocol:</p> <ul style="list-style-type: none"> • Observation of parent child interactions • Exploration of potentially effective strategies and contexts to embed goals • Demonstration of embedding goals and strategies • Guided feedback: caregiver practice with guidance and support from Interventionist • Reflection & problem solving of the whole exercise

	<p>Coaching protocol structure in video conference based sessions:</p> <ul style="list-style-type: none">• checking in with parent how the plan is going on at home• observation of routine chosen by parent to implement the goals and strategies• explanation & guided feedback on parents' skills and child's responses with suggestions of enhancements• coaching of new topics if earlier targets for caregiver competency achieved• setting goals as parent and child progress in their skills• Closing: recap proceedings of the sessions and plan for next session
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