PROTOCOL TITLE:

Lifestyle Enhancement for ADHD Program (LEAP) Study

PRINCIPAL INVESTIGATOR:

Erin Schoenfelder Gonzalez, Ph.D.
Center for Child, Health, Behavior, Development
206-987-2161
Erin.Schoenfelder@seattlechildrens.org

Pooja S Tandon, MD, MPH
Child Health, Behavior, and Development
206-884-1130
Pooja.tandon@seattlechildrens.org

Table of Contents

1.0 Objectives

1.1 Describe the purpose, specific aims, or objectives.

Purpose: Increase physical activity (PA) in children with ADHD using a novel, family-based intervention that promotes PA within the context of evidence-based behavioral management training (BMT) for parents, enhanced with mobile health (mHealth) behavior change strategies.

Specific Aims:

1) Test the feasibility and acceptability, of an 8-week, family-based, multi-level intervention (BMT-Health) to promote PA in young children with ADHD

2) to derive an estimate of the effect size of the intervention on PA

1.2 State the hypotheses to be tested.

The BMT-Health intervention will be feasible and acceptable to families for children with ADHD and will show promise for increasing PA in children with ADHD

2.0 Background

2.1 Describe the relevant prior experience and gaps in current knowledge.

Dr. Schoenfelder Gonzalez (Co-PI) is a clinical psychologist with expertise in psychosocial treatments and health risk behaviors associated with ADHD. She has published on the relationship of ADHD to health risk behaviors,[61] and on health promotion strategies for this population.[61-63] She has worked on RCTs of behavioral interventions for ADHD and published outcomes research on prevention programs for high-risk youth.[64-66] She collaborated with Dr. Mendoza (co-I) to complete a study using the proposed technological and social media components of the BMT-Health intervention (wearable activity tracker, Facebook engagement intervention) that was found to increase PA in adolescents with ADHD across a 4-week period.[14]

Dr. Tandon (Co-PI) is a general pediatrician and PA researcher with a K23 Career Development Award focused on promoting PA and outdoor time in early childhood, with an emphasis on the neurocognitive benefits of PA. She and her team have considerable experience collecting data via accelerometry and in community based interventions to promote PA in children. This work formed the basis of an R21/R33 application that was funded and will support a PA intervention in preschool children using mHealth technology.

2.2 This study will combine the use of mHealth wearable technology (Garmin vivofit) for children and caregivers, with a social media program (Facebook group) for caregivers, delivered through and integrated in a BMT program for a technologically and theoretically integrated, multi-level intervention approach. This proposal

represents the first study examining such an intervention to increase PA levels and improve health and functioning in children with ADHD.*See section 2.2 for details of team's prior research.Describe any relevant preliminary data.*

National Survey of Children's Health: Using nationally representative data from two time points over the past decade, we found that children with ADHD are at high risk for engaging in inadequate PA.[11] Only about a third of children with ADHD were reported to have had 20 minutes/day of MVPA in the previous week. Also, less than half of children with ADHD participated in sports in the past year. Children with more severe ADHD, lower SES, and obesity had lower odds of sports participation, which is not surprising but concerning, as these children are also at higher risk for co-morbidities and health disparities. Of note, medication use in ADHD was not associated with sports participation or achieving daily PA. Our findings highlight the need to focus on children with ADHD as a high-risk group for poor health behaviors. The abstract for this study has been accepted for presentation at the American Academy for Child & Adolescent Psychiatry Annual Meeting in 2017, and this paper is currently under review.

Clinic survey results: We developed and piloted a self-report survey data from 44 caregivers of children being seen for ADHD concerns in the Program to Enhance Attention Regulation and Learning (PEARL Clinic) at Seattle Children's Hospital. The measure was administered to all families seen for new evaluations in the PEARL Clinic during a 2-month time frame in the spring of 2017. Less than 12% of parents reported that their children engaged in >60 minutes of PA/day on 7 days/week. Seventy-six percent of parents reported that their child had 2 or fewer day of physical education at school/week. The most commonly identified barriers for their children to engage in PA activity were 1) does not do well in groups/needs 1:1 supervision, 2) not enough time, and 3) no interest (by child). Only 33% of responding parents reported that they themselves achieved the 150 minutes/week of PA recommended for adults. Eighty-one percent of parents said they would be potentially interested in participating in a program to increase their child's PA, and 88% said they would be interested in an activity tracker for their child. These survey results highlight both need for, acceptability, and local interest in a PA intervention for our families with children who have ADHD.

Teen ADHD Fitbit study: Drs. Schoenfelder Gonzalez (PI) and Mendoza (co-I) recently published a pilot study of an intervention to increase PA in adolescents (ages 14-18) with ADHD. Participants wore an activity tracker paired with a smartphone app, participated in a Facebook group, and received brief health coaching focused on PA goal setting. Across 4-weeks, adolescents significantly increased their daily PA, and trends were observed of improvement in self- and parent-reported ADHD symptoms.[14] Dr. Mendoza has also completed pilot trials of the proposed technological methodology (activity tracker, Facebook group, accelerometry

measurement), finding good feasibility and acceptability in non-clinical groups of adolescents[72] and adolescent cancer survivors.[15]

2.3 *Provide the scientific or scholarly background for, rationale for, and significance of the research based on the existing literature and how will it add to existing knowledge.*

Attention Deficit Hyperactivity Disorder (ADHD) is a common pediatric disorder associated with persistent and wide-ranging impairments and negative health outcomes, including obesity and Substance Use Disorders (SUDs). An estimated 5-10% of children worldwide have ADHD, which is marked by inattention, impulsivity and/or hyperactivity, and confers risk for difficulties in social, academic, vocational, and home functioning throughout development.[1,2,18,19] ADHD is associated with health risks such as obesity, which in turn increases chronic health problems and mortality rates.[20,10] Though stimulant medications improve ADHD symptoms and functioning acutely in the majority of those treated, medication is not recommended as the first-line treatment for young children with ADHD.[22] Moreover, many youth do not tolerate or adhere to medication, there are concerns regarding diversion,[23] and longer-term outcomes of medication remain unclear.[3] Thus, there is a need for innovative, generalizable intervention approaches that could serve as alternatives or adjuncts to existing treatments and that show promise for altering longer-term developmental and health trajectories.

Physical activity (PA) enhances neurocognitive and self-regulatory development and has been found to decrease ADHD symptoms. There is an emerging but limited literature that both brief and sustained periods of PA are associated with improved executive functions,[24,25] which are frontal lobe processes such as response inhibition and working memory that are often compromised in ADHD[7] and feature prominently in theories of ADHD.[26] Children with ADHD who participate in moderate-to-vigorous PA (MVPA) in clinic and school settings demonstrate improvement on cognitive tasks measuring sustained attention, response inhibition, stimulus processing, response accuracy, and self-regulation,[27-32] and also exhibit fewer behavioral symptoms of ADHD and improved reading and math achievement.[5,33-35] One meta-analysis reported an overall medium effect size (Hedge's g=0.63) of PA on ADHD functional outcomes; effects did not vary by PA intensity but increased with PA duration.[36] In the only large-scale randomized trial of a PA-intervention for children with ADHD, a 31-minute before-school exercise program improved both parent and teacher ratings of ADHD symptoms across 12 weeks, indicating lasting effects of the intervention throughout the day.[35] It should be noted, however, that this trial did not objectively measure PA but instead relied on physical fitness as a proxy measure. Additionally, observational studies have documented a link between PA and "real word" functional outcomes such as scores on standardized achievement tests.[37,33] Thus, interventions to increase PA for

children with ADHD have demonstrated the potential to improve broader domains of functioning, offering an alternative or supplementary treatment to existing treatment approaches. An acceptable and feasible multi-level, family-based intervention to increase PA of children with ADHD has the potential to improve executive functioning, reduce ADHD symptoms, and promote health, with implications for longer term well-being.

A3. Children with ADHD are at particular risk for not meeting recommendations for daily PA. Although hyperactivity would seem to increase daily energy expenditure, children with ADHD have been found to have high prevalence of physical inactivity and obesity.[10] These children may encounter unique barriers to adequate PA and sports participation that are related to their diagnosis. For instance, children with ADHD exhibit increased rates of disruptive, noncompliant, and aggressive behavior and poor motivation.[1] Their parents are more stressed[38] and tend to use less effective and more negative, punitive, and inconsistent parenting approaches than parents of non-ADHD youth.[39] Moreover, parents of children with ADHD have high rates of ADHD, depression, and substance use disorders themselves,[40] complicating their efforts to implement effective parenting strategies to promote PA. As such, parents of children with ADHD may have considerable difficulty encouraging participation in PA and/or limiting their sedentary behaviors, such as media use.[41] In fact, parents may offer screen time to their child in order to get a break from parenting. Additionally, children with ADHD demonstrate greater rates of oppositional behavior and poor sportsmanship in recreational sports settings, interfering with their engagement and success in sports and reducing overall PA.[42]

A4. Parenting interventions have been shown to be effective in modifying child behavior and improving ADHD functional outcomes. Decades of research on behavioral treatments for children with ADHD indicate strongest support for interventions that target parents, caregivers, and teachers rather than children directly.[43,44] Behavioral Management Training (BMT) for ADHD teaches parents to implement contingency management procedures to target the behavioral and functional problems associated with ADHD, most often by using behavior change strategies such as special playtime, differential attention, praise, incentives, and effective consequences to foster child skill development and behavior change.[45] Such interventions yield reductions in children's oppositional and aggressive behavior, increase parent use of positive parenting strategies, and reduce parent criticism and conflict.[46,47] However, such programs focus primarily on reducing noncompliance and parenting stress, whereas no evidence currently exists on how these strategies impact health behaviors such as PA. Furthermore, such programs were developed over 30 years ago, prior to the internet, WIFI, and cultural changes affecting the current context of parent-child interactions. We hypothesize that enhancing and augmenting evidence-based BMT strategies (e.g., special playtime, praise,

incentive systems) to additionally target PA in ADHD youth will increase measured PA and subsequently yield even greater improvements in ADHD symptoms and overall functioning than current treatments alone.

Summary of Scientific Premise: Increasing PA is associated with improvements in executive functions, ADHD symptoms, and broader academic and social functioning.[5,34] **Therefore, family-based interventions to increase PA in ADHD youth could substantially improve ADHD-related functioning if integrated with existing evidence-based parenting interventions for ADHD, and may also reduce risk for negative health outcomes.**.

3.0 Inclusion and Exclusion Criteria

3.1 Describe how individuals will be screened for eligibility.
Prior to the screening visit, participants will complete a pre-screening interview over the phone with one of the study staff. The study staff will conduct the interview using a phone screen script. If the subject is eligible then potential participants and their caregiver will attend an initial screening visit to confirm ADHD diagnosis and global severity. Eligible children will then complete a two-step screening procedure for low PA participation (caregiver-report survey of daily PA and a 3-day accelerometer wear) to determine level of daily PA.

Describe the criteria that define who will be included or excluded in your final study sample.
Inclusion criteria for children:
- age 5-10 years
- ADHD diagnosis
- engage in <5 days of vigorous physical activity for more than 60 minutes at a time based on parent report
-CGI-S rating >4 and <7
-One adult caregiver willing to participate in the study and complete baseline/follow-up measures
Inclusion criteria (for participating caregiver):
- willing to participate in the study and complete baseline/follow-up measures
- able to complete forms in English
- owns a smart phone or similar Garmin compatible mobile device (e.g. iPod Touch) or willing to borrow iPod from study coordinators during the study period
-Agree to install and share data from the Garmin smart phone app with investigators
Inclusion criteria (for supplemental caregiver)
- caregiver to child already participating in study

Child Exclusion Crit*eria*:

- younger than *5 years old or older than 10 years old*
- do not meet criteria for ADHD diagnosis
- per caregiver report, engage in >60 min/day of MVPA consistently for at least 5 days per week
- Meet diagnostic criteria for psychiatric co-morbidities including Autism Spectrum Disorder, Depressive Disorder, Mood Disorder, Psychotic Disorder, or Intellectual Disability that could interfere with intervention uptake
- currently taking psychotropic medications that may decrease ability to engage in PA (e.g. Alpha 2 agonists during the day). Children receiving stimulant medications who are on a stable dose for the past 30 days will be eligible for participation
- any physical or medical restrictions on PA

-Child currently/previously used a wearable physical activity sensing device the majority of days for a 2 month period in the past year

Caregiver Exclusion Criteria:

- Caregiver participated in an evidence-based parent behavior management training program (i.e., Incredible Years, Triple P, PCIT, Barkley's Defiant Child) in the past 24 months.

3.2 *Indicate specifically whether you will include or exclude each of the following special populations: (You may not include members of the above populations as subjects in your research unless you indicate this in your inclusion criteria.)*

- *Adults unable to consent* - excluded
- *Individuals who are not yet adults (infants, children, teenagers)* - included
- *Wards of the state* - excluded
- *Pregnant women* - Excluded
- *Prisoners* – excluded

3.4 Screening Visit

Screening visits will be completed within 60 days of group treatment start. Eligible participants will be enrolled on the same day as the screening visit.
Diagnostic evaluation will consist of structured interviewing with the child and caregiver on the *Schedule for Affective Disorders for School-Aged Children (K- SADS) Present and Lifetime Version (K-SADS-PL)*,[35] which assesses current and past presence of DSM-5 disorders in ages 6-18. Interviewing will be completed by a licensed psychologist or supervised pre- or post-doctoral trainee. The K-SADS-PL has strong test-retest and inter-examiner reliability, with kappas for ADHD above .70.[36] Inter-examiner reliability will be established and monitored over the trial by taping interviews and randomly selecting 20% for reliability checks. Should kappas fall < .70, additional training will be provided.

The *Clinical Global Impressions (CGI-S) ADHD Severity Scale,[37]* a clinician-rated, 7-point scale that describes the severity of ADHD symptoms (using the K-SADS), will be used to screen for ADHD severity. Children must have a current CGI-S rating >4 to participate. The CGI-S also serves as an exploratory outcome in the R21 phase and a secondary outcome in the R33 phase.

4.0 Study-Wide Number of Subjects

4.1 N/A

5.0 Study-Wide Recruitment Methods

N/A

6.0 Multi-Site Research

N/A

7.0 Study Timelines

7.1 Describe:

- *The duration of an individual subject's participation in the study.*
  For participants in the BMT-Health group intervention – approx. 9 - 16 weeks from the date of screening/baseline enrollment
- *The duration anticipated to enroll all study subjects.*
  Using a rolling recruitment approach, enrollment for the entire study is anticipated to take 2 years.
- *The estimated date for the investigators to complete this study (complete primary analyses)*
  The estimated date for completion of this study is January 2020.

8.0 Study Endpoints

8.1 Describe the primary and secondary study endpoints.
The study endpoint is the completion of all subjects' participation in the study intervention and completion of all data collection and analysis.

8.2 Describe any primary or secondary safety endpoints.
N/A

9.0 Procedures Involved

9.1 *Describe and explain the study design.*
LEAP Group Intervention
At the beginning of the screening visit, informed consent/assent forms will be reviewed aloud with participants. Screening consists of completion of the K-SADS and physical activity screening questionnaire. Children eligible based on these measures will then complete PA tracking using accelerometer as described in section 3.1 Following screening into the

study and completing informed consent/assent and baseline study measures, caregivers will be assigned to an 8-week LEAP intervention group, with 6-8 caregivers per group. Children and caregivers will complete baseline and follow-up assessment batteries at 5 weeks and 9 weeks. Caregivers will participate in a 1-hour focus group regarding their experience in the intervention during week 9. PA will be measured using accelerometry x7 days at baseline and at 9 weeks. The LEAP intervention consists of 3 components: 1) an enhanced 8-week, group-based BMT curriculum, 2) caregiver and child use of the Garmin daily activity tracker accompanied by personalized goal setting, and 3) caregiver participation in a private Facebook group to encourage PA goal achievement and promote social support and positive parenting. All enrolled families will receive 8 weekly group BMT-Health sessions led by either Dr. Schoenfelder-Gonzalez or Dr. Sasser, who have considerable experience leading BMT groups for children with ADHD. Groups will include initial enrollment of 6-8 families, a group facilitator, and a co-facilitator. The curriculum and homework is based on existing evidence-based models, namely Barkley's Defiant Children[12] curriculum, with integrated content specifically focused on promoting PA and addressing barriers to PA. Table 1 presents a sampling of session content, highlighting the unique aspects of the BMT-Health curriculum compared to standard BMT. Later sessions (with related homework) will include topics such as: community resources for PA, challenges encountered and over-coming barriers, using incentives to promote healthy behaviors, role of bedtime routines/sleep, and goal-setting for the future/strategies for sustainability. Information and resources relevant to that week's topic will also be provided via Facebook and text messages. Fidelity to the curriculum will be assessed by trained coders using content checklists in a randomly-selected sampling of session audiotapes. We included the standard Barkley curriculum with this IRB application. We now include an overview of LEAP curriculum sessions 1-8 and how the sessions are similar to and differ from the Barkley curriculum (see separate attachment).

Table 1. BMT Standard and BMT-Health Curricula Overview – Sessions 1-3.

Barkley's *Defiant Children*[12]			**BMT-Health**		
Strategy Instruction	Homework	Session	**Unique** Strategy Instruction	**Unique** Homework	**Unique** Targets
• Psychoeducation: ADHD and causes of child misbehavior • Teach differential attending and "special time" strategies	• Daily "special time" play	1	• Psychoeducation: ADHD/misbehavior and connections with PA and health behaviors • Teach incorporation of active play into daily "special time" • Distribute and teach caregivers to use Garmins	• Daily "special time" with active play • Caregiver & child wear Garmin	• Child and caregiver engage in active (Non-sedentary) play together • Child and caregiver monitor activity levels
• Continue "special time" practice and planning • Teach praise/ reinforcement of	• Continue "special time" • Praise child	2	• Discuss PA successes. Identify and problem-solve barriers. • Teach caregiver self-care strategies (e.g., own PA, sleep,	• Set individual child and caregiver PA goals based on prior week's Garmin results	• Establish individualized goals for PA • Increase

compliance	compliance		self-talk, social support) • Introduce caregiver Facebook group	• Join and participate in Facebook group	caregiver PA and social support via Facebook group
• Teach effective commands and limit setting (i.e., rules, when/then commands, timers)	• Use effective commands, limit setting strategies	3	• Teach limit setting strategies applied to PA and rules for media use • Psychoeducation: media use and ADHD	• Develop and implement family media use plan • Use effective limit setting to support family media use plan	• Reduce child and caregiver media use • Replace sedentary activity with active play

9.2 *Provide a description of all research procedures being performed and when they are performed, including procedures being performed to monitor subjects for safety or minimize risks. Please be clear about how the procedures performed differ from standard of care. If procedures preclude or delay standard of care, please be sure to include this information.*

Garmin Wrist-worn Activity Tracker – Vivofit Jr; The Garmin vívofit jr is a wrist worn activity tracker intended for children ages 4 to 9 years old. It has a 1+ year battery life, is waterproof, and tracks steps and PA with a built in tri-axial accelerometer. The child-friendly displays shows step count and whether the "activity goal" of >60 minutes was met. Caregivers can use a compatible application on their Apple or Android smartphone to monitor the activity of up to 8 family members. The device can store data for 4 weeks. For the caregivers, we will use an adult oriented wrist-worn product, the Garmin vívofit4, which has a1+ year battery life and a digital display with steps, PA duration and intensity, and a “move bar” which alerts them to move. Participants will be encouraged and supported in setting personalized goals based on their actual PA data collected by the Garmin in week 1 and incrementally increase activity to meet and maintain population recommendations for their age. Using a texting platform, we will set up automated weekly texts to go out to participating caregivers with reminders and goals. The content of the texts will be submitted to the IRB prior for review prior to using them in the study. The weekly texts will continue until the last data collection period at each phase of the study. Intervention participants will be encouraged to share their Garmin data on their own personal social media profile with their online friends and other study participants. Participants will also receive brief health coaching regarding PA goal setting each week with study staff, which has been found to be effective in other PA interventions.[9]

BMT group based curriculum - BMT programs – such as Barkley’s Defiant Children[12] – are front-line treatments for childhood ADHD,[13] and focus on issues such as reducing noncompliance and parenting stress. We propose to enhance Barkley’s program to target PA via BMT strategies such as special time, praise, and incentive systems, which we hypothesize will increase PA and yield greater improvements in ADHD symptoms and

functioning than existing BMT programs or stand-alone interventions providing structured PA sessions.

Facebook Group.
We will create a private (invitation only) Facebook group for each LEAP intervention group to provide encouraging advice and messages to promote PA, announce weekly individual and group badges/awards (e.g., most improved, most steps, most active minutes, most Facebook posts, etc.), and to provide a forum for participants to discuss PA and use of the Garmin devices. A group facilitator profile will be created with which research assistants can post to the group page, interact with participants, and screen content posted by members daily to remove it if inappropriate. The facilitator will make about 5 posts per week providing encouragement, reminders and study procedures, and opportunities to troubleshoot and answer questions. We have included a manual with information on planned posts. Participants will earn digital badges for meeting their weekly activity goals, as well as for social interactions (e.g."liking" other's posts) or making improvement toward goals to ensure that all participants receive positive feedback. We will begin the first 4 weeks with badges awarded to individuals only (e.g. most improved individual, most steps (from baseline) for an individual, etc.). Starting in week 5, we will award additional badges contingent on the entire intervention group meeting pre-specified criteria (e.g. 250,000 steps attained). This "all for one and one for all" approach is designed to foster encouragement and cooperation among the participants to promote PA and to keep participants engaged. Participants will be encouraged but not required to post in the group and to encourage their fellow participants. Participants will also receive standardized weekly text messages (using a free service) reminding them to wear/sync their Garmin and increase PA in their family routines. The facilitator and investigators will build upon the operations manual used in our teen ADHD pilot study to add practical information and troubleshooting tips for the purposes of training and guiding others to fulfill the role as independently as possible. Facilitator will track time spent each week as an indicator of implementation burden.

Questionnaires/Measures – listed in Table 2; completed by teachers, caregivers, child participants, or therapists. Of the measures listed below, we will submit the HBD for IRB approval prior to administration.

- Hip –worn Accelerometer – Actigraph model GT3X+; A small rectangular device housing a tri-axial accelerometer and worn on an elastic belt, the GT3X+ has been used in a number of studies conducted by Dr. Tandon's (Co-PI) research group and a number of other research groups at Seattle Children's. Children will be asked to wear the device with an elastic belt for 7 days on their hip. In order to maximize valid accelerometer data, participants will be asked to wear accelerometers for 24 hours/day, except for water-based activities,[38] and to re-wear accelerometers for another 7-day period if they have < 4 valid days at each measurement time point. The 24-hr wear has been validated for use to collect sleep data in school age

children, which is an exploratory outcome in this study.[39] While sleep has traditionally been measured with wrist actigraphy, algorthims have been produced, validated, and refined to fully automate the capture of sleep duration for children using 24-hour waist-worn acclerometry.[40] As we plan to use a 24-hour waist-worn accelerometer protocol to maximize compliance for the PA data, we will also be able to capture quantitative sleep data on our participants for a broader perspective on these related health behaviors.

Digit Span task asks children to repeat strings of numbers of increasing length forward, then backwards.

- *Stop Signal Reaction Time (SSRT):* In this computerized task, the participant must respond to an arrow stimulus, by selecting one of two options, depending on the direction in which the arrow points. If an audio tone is present, the subject must withhold making that response (inhibition). The test consists of two parts:
  In the first part, the participant is introduced to the test and told to select the left-hand button when they see a left-pointing arrow and the right-hand button when they see a right-pointing arrow. There is one block of 16 trials for the participant to practice this.
  In the second part, the participant is told to continue selecting the buttons when they see the arrows but, if they hear an auditory signal (a beep), they should withhold their response and not select the button. The total task requires 15-20 minutes to complete.

Table 2 – Study Measures and Assessments

Construct	Measure	Rater	Source	Screening	Baseline	5 weeks	9 weeks
ADHD diagnosis	K-SADS-PL	P/C	CR	X			
ADHD severity	CGI-S	Clinician	CR	X			X
PA, Sleep	MVPA, light & sedentary time, Step count, sleep duration x 7 days	G/C/A	E		X		X
Feasibility	Garmin (wear time), Facebook likes and comments	G/P/C	E, SE			X	X
Acceptability	Attendance, TAI	P	CR, DP			X	X
Acceptability	CSQ, Focus group		DP				X
Executive function	SSRT, DS, BRIEF-2	C/P	SE		X		X
ADHD symptoms	Conners-3 (P), Vanderbilt (T)	P/T	DP		X		X
Functional impairment	IRS	P/T	DP		X		X
Parenting	APQ	P	DP		X		X
PA, Sleep, Media use	HBS	P	DP		X	X	X
Sleep problems	CSHQ	P	DP		X		X
BMI	Height, weight	C	SE		X		X
Complementary/Alternative medicine use	HBS	P	DP		X		X
Media Use	Problematic Media Use	P	DP		X		X
Medication use	HBS	P	DP		X	X	X
Mindfulness	Mindful Attention Awareness		DP		X	X	X

	Scale						
Socio-demographics	Survey	P	DP		X		

APQ = *Alabama Parenting Questionnaire*. BMI = Body Mass Index. BRIEF = *Behavior Rating Inventory of Executive Function*. CGI-S = *Clinician Global Impressions Scale – Severity*. Conners-3 = *Conners–Third Edition.* CSHQ = *Children's Sleep Habit Questionnaire*. CSQ = *Client Satisfaction Questionnaire*. DS = *Digit Span* task. ERC = *Emotion Regulation Checklist*. FW = *Finger Windows* task. HBS = *Health Behaviors Survey*. IRS = *Impairment Rating Scale.* K-SADS-PL = *Kiddie-SADS-Present and Lifetime Version.* MVPA = Moderate-to-Vigorous Physical Activity; PA = Physical Activity. SSRT = *Stop-Signal Reaction Time* task. TAI = *Treatment Adherence Inventory*. A = Actigraph GT3x+; C = Child; G = Garmin Device; P = Parent; T = Teacher. DP=digitally entered by parent/caregiver; CR=Clinician rated; E=electronic device data; SE =study staff entered

For the K-SADS instrument:

- the Pregnancy and Birth Questions will not be included
- the Family History for Biological Relatives will not be included

10.0 Data and Specimen Banking

N/A

11.0 Data Analysis/Management

Describe the data analysis plan, including any statistical procedures.

Given the pilot nature of the R21 study, data analysis will be largely descriptive and exploratory. We will focus on parameter estimates instead of formal hypothesis testing. The feasibility and acceptability of the research protocol as outlined above is the main outcome of interest, as is now recommended for pilot studies, rather than effect size estimates.[109]

Study aim 1: To test the feasibility and acceptability of the intervention

Feasibility will be assessed by (a) demand through inquiry and enrollment rates and (b) practicality and participation through attrition rates and adherence with intervention (attendance, percentage of days wearing and syncing Garmin, participation in Facebook group) and study procedures (screening, follow-up batteries, accelerometry). Acceptability will be assessed through participant ratings and qualitative interviews. Fidelity of the social media/text component will be evaluated following a procedure for prior mHealth intervention pilots conducted by the study team including tracking facilitator posts, participant views, likes, and posts. We will summarize the measures listed above using means, medians, and standard deviations for continuous variables and proportions for categorical variables and then conduct bivariate analyses. Non-parametric tests will be used on non-normally distributed continuous variables, and Fisher's exact test on sparse categorical variables. The proportions that reflect acceptability and feasibility will be assessed using 95% exact (Clopper-Pearson) confidence intervals

Exploratory Aim: To explore the effects of the intervention on PA

We will compare within-subject pre to post activity using accelerometer data (step count; sedentary, light and MVPA; sleep duration), MVPA as an exploratory outcome. We will examine gender as an effect modifier given that differences in PA are seen between boys and girls from an early age and differential effects of previous PA interventions by gender have been noted.(111) We will also look at associations of the measures from Aim 1 with PA outcomes. Pre- and post-intervention outcomes will be compared using t-

tests, paired t-tests, chi-square and when appropriate, Fisher's exact test. We will account for within-subject correlation due to repeated measures. Due to the pilot nature of the intervention, we emphasize the analyses will be primarily descriptive; confirmatory analysis will await future studies.

11.1 Provide a power analysis.

We anticipate needing to screen up to 45 children for low PA to ensure enrollment of 30 eligible families, but will screen more if needed. Treatment groups will begin on a rolling basis as soon as 6-8 eligible families have enrolled.

11.2 Describe any procedures that will be used for quality control of collected data.

N/A

12.0 Confidentiality

12.1 Describe the steps that will be taken to secure the data or specimens (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission.
We will take the following steps to ensure data will be secure during storage, use, and transmission: proper and consistent training of staff members, limit authorization of access to study team members, password protect the electronic data files, physically lock forms with identifiable information in a locked cabinet in staff offices, and ensure separation of identifiers and PHI data.

12.2 Describe how data and specimens will be managed study-wide

Staff will be informed of the need for confidentiality as information to be obtained will contain PHI (e.g. name, DOB, contact information, basic demographic info). Forms with identifiable names will be kept in a locked cabinet room in staff offices at SCRI. The electronic data files will not have any personally identifying names in the file, and will kept on a secure HIPAA compliant server hosted by Children's for a minimum of 6 years. Digitally audio recorded interviews will be deleted following transcription and will not be kept on file. No names or addresses will be reported in publications. Only the PI, research coordinator, and research administrator have keys to the offices and locked cabinets at SCRI.

13.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

13.1 Describe:

Prior to implementing the study, the protocols, information sheet, recruitment materials and evaluation procedures will be reviewed by Seattle Children's Institutional Review

Board. Any adverse events will be recorded and reviewed by the PIs (Dr. Tandon, Dr. Gonzalez) and their study team. Any adverse event and the actions taken will be reported to the IRB at Seattle Children's Research Institute.

A two-person DSMB will be established for the proposed study who will advise the study investigators. The DSMB is comprised of (1) a pediatrician and NIH-funded investigator studying early childhood development (Dimitri Christakis, MD), and (2) a psychiatrist and specialist in child and adolescent and mental health including ADHD , William French, MD, Professor of Psychiatry & Behavioral Sciences at the University of Washington. Neither of the DSMB members are investigators or key personnel of the proposed research study, but all have expertise for essential components of the intervention.

The primary responsibilities of the DSMB will be to (1) periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and (2) make recommendations to the PI and co-investigators concerning the continuation, modification, or termination of this study. The PI and co-investigators will report any serious unexpected adverse event (whether associated with the intervention or not) to the DSMB, IRBs, and NIH within 48 hours by telephone and within 5-working days in writing. The DSMB and IRBs will also determine whether the adverse event is causally related, probably related, possibly related, or unrelated to the intervention. A serious unexpected adverse event is provisionally defined as any of the following:

a) death
b) any acute life-threatening event, including any serious physical activity-related injuries
c) any event requiring hospitalization or emergency department care
d) any other event that warrants a designation of a "serious" event in the PI's, Co-Is', or DSMB's judgment, including threats to safety or "near-miss" injury events that could have led to items a-c above

All other adverse events will be filed annually with the DSMB, the IRBs, and the NIH. Routine monitoring for adverse events will be performed by the study staff and coordinators, the PIs, and co-investigators. Since there are no investigational drugs or devices, there will be no routine post-study follow-up of participants.

Should a Caregiver or child enrolled in the study report concerning information related to suicidal ideation or safety in the course of their participation, Dr. Gonzalez will meet with the family individually to further assess concerns, engage in safety planning as needed, and connect the participant with mental healthcare or emergency services. Regarding medical symptoms related to exercise, we will contact the participant's family and refer the child or parent for the appropriate medical attention with the family's primary care provider.

14.0 Withdrawal of Subjects

14.1 Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent.

We do not anticipate conditions where subjects will be withdrawn from the research without their consent.

14.2 Describe any procedures for orderly termination. N/A

14.3 Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection.
Should subjects withdraw from the research, we will keep their data (unless requested otherwise from subject) for later analyses. Like all other data to be analyzed, subjects who withdraw will have their data de-identified and kept on HIPAA compliant servers. As much as possible, we will remove content posted by the participant from the Facebook group and direct the participant to delete the Garmin app.

15.0 Risks to Subjects

15.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research. Include as may be useful for the IRB's consideration, describe the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, and economic risks.
There are no drugs or devices used in this study. This is a minimal risk study that has no potential serious harms or risks related to participating in this study. Study procedures may include possible participant discomfort as discussing personal experiences and opinions may become emotional for participants. To avoid or mitigate any psychological risks, research staff will be trained to provide appropriate support and help participants calm in the even that s/he becomes emotional. Participants may also be offered a break and reminded that they can take as much time as needed. Subjects may feel some discomfort wearing the Garmin wrist activity tracker or the Actigraph hip-worn activity meter but these devices are designed for daily use and have been used by our research group (and others here at Seattle Children's) without major incident. The Facebook page will be monitored each weekday by study staff in order to ensure that inappropriate language or behavior between study participants is identified.

15.2 If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable.
N/A

15.3 If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant.
N/A

15.4 If applicable, describe risks to others who are not subjects.
For others who are not subjects (e.g. other family members not participating in the study), there may be risk of emotional or social discomfort should participant discuss challenges related to group participation (e.g., discussion of ADHD-related difficulties) or use of program skills at home

(implementation of consequences, rewards), or inconvenience of accommodating lifestyle changes to increase PA caused by the program.

16.0 Potential Benefits to Subjects

16.1 Describe the potential benefits that individual subjects may experience from taking part in the research. Include as may be useful for the IRB's consideration, the probability, magnitude, and duration of the potential benefits.

Potential benefits to subjects may include increase in PA, as well as a decrease in ADHD symptoms and associated behavioral difficulties through participation in the BMT program.

17.0 Vulnerable Populations

The research is minimal risk as child participants will not be engaging in any activity that carries significantly greater risk than what they would likely already be doing as a child. Wearing the activity tracker does introduce monitoring of activity so it is possible that they may feel encouraged to be more active. Children's caregivers may provide additional opportunities for physical activity but these would unlikely significantly increase their level of risk.. Adult participants will not be prescribed any intense physical activity as part of the study. The activity meter is worn on a soft elastic belt and has been used in several other studies within our research group and department without incident. We have used similar versions of the Garmin Vivofit activity tracker in previous research studies with no issues or complaints.

18.0 Community-Based Participatory Research

N/A

19.0 Sharing of Results with Subjects

Data analysis, manuscript writing, publications, and presentations will all be derived from de-identified data; all research products (e.g. publications, presentations) will be double checked for possible identifying information prior to submission. Results and research products will be shared with participants once finalized post analyses and publication.

20.0 Setting

20.1 Describe the sites or locations where your research team will conduct the research.

Potential subjects will be identified and recruited through primary care and specialty clinics affiliated with Seattle Children's Hospital. Screening visits and BMT program meetings will take place at the Seattle Children's main campus in Seattle, WA.

21.0 Resources Available

21.1 Describe the qualifications (e.g., training, education, experience, oversight) of you and your staff as required to perform their role. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research.

The PIs of the study include a clinical psychologist with expertise in psychosocial treatments and health risk behaviors associated with ADHD (Schoenfelder) and a general pediatrician and PA researcher with a k23 Career Development Award focused on promoting PA and outdoor time in early childhood (Tandon).

The CRA for the study has extended experience working with accelerometry data and Garmin wearable technology.

21.2 Describe other resources available to conduct the research: For example, as appropriate:

- *Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?*

  We will recruit participants through primary care and specialty clinics affiliated with Seattle Children's Hospital. This strategy was effective in several prior studies conducted by the study team. Within the PEARL Clinic, an ADHD specialty clinic within outpatient psychiatry, 484 unique patients were seen in 2016, of which 210 were ages 6-8 years. Medical and mental health providers will be asked to disseminate study information to ADHD-diagnosed youth under their care in the PEARL Clinic and outpatient psychiatry. Since the majority of youth with ADHD are treated in primary care, we will also distribute study information to local primary care clinics. Co-PI Tandon is a provider in the Roosevelt Clinic through UW, where she can coordinate recruitment efforts. Advertisements via Facebook, one of the platforms to be used in the intervention, and through the Seattle Children's Hospital and Seattle Children's Research Institute website will be used if needed. These methods have worked well in prior studies by the co-PIs and Co-Is. If such advertisements are needed, we will submit the proposed ad to the IRB for approval.

  Describe the time that you will devote to conducting and completing the research.

The grant provides for protected time for the PIs and Co-Is to conduct the proposed research.

- *Describe your facilities.*
  Assessments and study groups will be conducted at Seattle Children's Hospital. The co-PI (Schoenfelder) and several of the Co-Is (Stein, Sasser) have offices there. There are private treatment and group rooms available for the study.

- *Describe the availability of medical or psychological resources that subjects might need as a result of an anticipated consequences of the human research.*

  Physical activity it taking place in the participants' own homes and neighborhoods. We will refer patients to consult regarding fitness-related concerns or injuries with their primary care doctor. The need for additional psychological resources will be assessed by the Co-PIs or Co-Is. Emergency services are available at Seattle Children's. We will facilitate referrals for individual mental health treatment within Outpatient Psychiatry or in the community if needed.

- *Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.*

  Upon hiring, the co-PIs will provide training in the study protocol to all hired research assistants or other personnel working on the study. Job descriptions will be provided prior to hiring. The co-PIs will supervise all personnel on the study.

22.0 Prior Approvals

N/A

23.0 Recruitment Methods

23.1 Describe when, where, and how potential subjects will be recruited.

Subjects will be recruited through a Seattle Children's Hospital-based specialty ADHD Clinic and primary care clinics associated with Seattle Children's (Roosevelt clinic; Harborview Primary Care). One of the Co-PIs (Schoenfelder) is a provider in the Program to Enhance Attention Regulation and Learning (PEARL) Clinic in Outpatient Psychiatry at SCH, the other Co-PI (Tandon) is a provider at the Roosevelt Clinic, and one of the Co-Is (Mendoza) is a provider at Harborview Primary Care . Within the PEARL Clinic, 484 unique patients were seen in 2016, of which 210 were ages 6-8. Medical and mental health providers will be asked to disseminate

study information via a study flyer to ADHD-diagnosed youth under their care in PEARL and outpatient psychiatry. We will send letters to families on the PEARL Clinic wait list and former PEARL Clinic patients. We will also have a study description in the PCP referral system to the PEARL Clinic, so PCPs will see a description of the LEAP study in the list of studies that get faxed back to PCPs when the PEARL Clinic not accepting new referrals. Because the majority of youth with ADHD are treated in primary care[85], we will also distribute study information to the Roosevelt associated with Seattle Children's to be posted in waiting areas and given to providers to distribute to patients with ADHD. Recruitment will take place during the first phase of the project and will be rolling until all treatment groups have been filled.

23.2 Describe the source of subjects.

Please see above for information regarding the PEARL clinic and primary care clinics, as well as Facebook/Instagram advertisements.

23.2 Describe the methods that will be used to identify potential subjects.

Providers will be asked to distribute study flyers to patient with ADHD diagnosis or probable ADHD. Flyers will direct interested families to a website customized for the present study, which will connect them with study staff for further information. The website will contain only study title, purpose of study, protocol summary, basic eligibility criteria, study site locations, how to contact the study site for more info. The Facebook/Instragram ad (to be submitted via Modification) will be run three times weekly during the recruitment period, directed at users who are caregivers of school-aged children. The link will direct interested individuals to a study website with contact information for the study coordinator.

23.3 Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For printed advertisements, attach the final copy. For online advertisements, attach the final screen shots (including any images). When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)

Facebook/Instragram advertisement will be submitted via modification. If the participant consents to participate in the study then information collected during the pre-screening phone call will be kept in a locked cabinet. If the participant does not wish to participate or does not sign a consent form then the information collected during the pre-screening interview will be destroyed.

23.4 Describe the amount, method (e.*g. gifts, check, gift cards) and timing of any payments to subjects. Provide details on who will be the recipient of the payment (caregiver or child).*

For each assessment visit (screening visit, Baseline, 5 week and 9 week assessments), subjects will will receive parking validation. Participants will receive compensation for completing study assessments in the following amounts: (1) $15 for screening visit and completion of accelerometry screening; (2) $25 for baseline battery completion (3) $25 for Week 5 (4) $50 for week 9 (5) $15 for participating in focus group. Supplementary caregivers will not receive any payment for participating. The amount will total $130 per family. Up to $20 will be provided for each group session for families that need to purchase childcare, totaling up to $160 per family for childcare reimbursement. Teachers will be reimbursed $10 for each of the two questionnaire batteries they are asked to complete (baseline and 9 weeks).

24.0 Use of Social Media

Facebook Advertisements: As described above, we will recruit for the study using Facebook advertisements targeted at caregivers of school-aged children. This advertisement will be submitted via modification.

BMT-Health Facebook Group: We will create a private (invitation only) Facebook group for each BMT-Health intervention group to provide encouraging advice and messages to promote PA, announce weekly individual and group badges/awards (e.g., most improved, most steps, most active minutes, most Facebook posts, etc.), and to provide a forum for participants to discuss PA and use of the Garmin devices. A group facilitator profile will be created with which research assistants can post to the group page, interact with participants, and screen content posted by members daily to remove it if inappropriate. The facilitator will make about 5 posts per week providing encouragement, reminders and study procedures, and opportunities to troubleshoot and answer questions. Participants will earn digital badges for meeting their weekly activity goals, as well as for social interactions (e.g."liking" other's posts) or making improvement toward goals to ensure that all participants receive positive feedback. We will begin the first 4 weeks with badges awarded to individuals only (e.g. most improved individual, most steps (from baseline) for an individual, etc.). Starting in week 5, we will award additional badges contingent on the entire intervention group meeting pre-specified criteria (e.g. 250,000 steps attained). This "all for one and one for all" approach is designed to foster encouragement and cooperation among the participants to promote PA and to keep participants engaged. Participants will be encouraged but not required to post in the group and to encourage their fellow participants. Participants will also receive standardized weekly text messages (using a free service) reminding them to wear/sync their Garmin and increase PA in their family routines. The facilitator and investigators will build upon the operations manual used in our teen ADHD pilot study to add practical information and troubleshooting tips for the purposes of training and guiding others to fulfill the role as independently as possible. Facilitator will track time spent each week as an indicator of implementation burden.

All Facebook group content and text messages will be submitted for approval via modification prior to contact with participants.

25.0 Local Number of Subjects

We aim to recruit 45 families (child, accompanying parent, and any supplemental caregivers) to ensure a total of 30 families will be enrolled after the screening process.

26.0 Provisions to Protect the Privacy Interests of Subjects

26.1 *Describe the steps that will be taken to protect subjects' privacy interests. "Privacy interest" refers to a person's desire to place limits on whom they interact or whom they provide personal information.*
This is a minimal risk study that has no potential serious harms or risks related to participating in this study. Study procedures may include possible participant discomfort as discussing personal behavioral health information may become emotional for participants.

All screening materials and interview files/transcripts will be de-identified prior to analysis. Participants will have their own study ID. The key of participant study IDs matched to names and other identifiers collected during recruitment will be kept in a separate password protected database. Only select study staff (e.g. data manager, study coordinator, PI) will have access to the key. Data analysis, manuscript writing, publications, and presentations will all be derived from de-identified data. All research products (e.g. publications, presentations) will be double checked for possible identifying information prior to submission.

26.2 Describe what steps you will take to make the subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures.
To lessen the burden on subjects, they will be interviewed in a private room at Seattle Children's; minors are welcome to have caregivers present upon request.

27.0 Compensation for Research-Related Injury

This research does not involve more than Minimal Risk to subjects and research is unlikely to result in injury.

28.0 Economic Burden to Subjects

Subjects will be responsible for their own transportation to Seattle Children's (Main Campus) for screening/study visits (e.g. fuel, childcare for other children). Upon arrival, parking will be free/validated for subjects. A $20 transportation reimbursement will be provided for each study visit.

29.0 Consent Process

29.1 Indicate whether you will you be obtaining consent, and if so describe:

Research staff (PI or research coordinator or research assistant) will obtain subject consent prior to conducting any study activities. The exception to this is the pre-screening phone call, study staff will ask potential participants questions to see if they are a good fit for the study. Consent will occur in private rooms at Seattle Children's Hospital or Seattle Children's Research Institute.

At the beginning of the screening, informed consent/parental *permission and/assent forms will be reviewed aloud with participants.* If supplemental caregivers will be participating, the supplemental caregiver consent form will also be reviewed. Adults will sign informed consent documents for their participation. If a family wishes to have a second caregiver participate in the groups, they will sign a separate consent form (IRB approved) to consent for group participation, though study data will not be collected from this caregiver. For children, caregivers will review and sign a caregiver permission form. Children who are 5-6 yo at time of enrollment will be asked to provide verbal assent (please see verbal assent script uploaded to Click). Children who are 7-10 yo at time of enrollment will be asked to sign an assent form. Participants will be invited to review the forms independently for as much time as desired and ask questions directly to the PI before signing. We will ask children to reiterate in their own words what they are asked to do and their right to decline to answer or withdraw from the study at any time to confirm comprehension.

We will be following the "SOP:HRP-090 informed consent process for research" protocol. As such, a copy of the signed consent form will be provided to subjects. This signed copy will be provided to families.

Non-English Speaking Subjects

Hint: please see HRP-090, HRP-091, and Investigator Manual HRP-103 for more information.

- *Indicate what language(s) other than English are understood by prospective subjects or representatives.*
- *If subjects who do not speak English (LEP participants) will be enrolled, please indicate whether you will be following the steps outlined in the Investigator Manual.*

All study participants will be English speaking. For the purposes of this pilot study, we are not able to obtain all measures in other languages, nor translate all other study materials. Many of our measures have not been validated in other languages.

Waiver or Alteration of Consent Process (consent/caregiver permission will not be obtained, required information will not be disclosed, or the research involves deception); Waiver or Alteration of HIPAA

- *Review the "CHECKLIST: Waiver or Alteration of Consent Process" and "CHECKLIST: HIPAA Waiver of Authorization" (HRP-410 and HRP-441) to ensure you have provided sufficient information for the IRB to make these waiver determinations.*
    - *Waivers for recruitment*
    - *Waivers for participants who turn 18*
    - *Waivers for information collected about a non-present caregiver*
    - *Other waivers as necessary*

A waiver of HIPAA authorization and alteration of the consent process (caregiver permission) is requested to complete the pre-screening phone call. The purpose of the phone call is to provide caregivers with more information about the research study as well as ask preliminary questions to determine if the family is a good fit to bring in for a screening visit. Caregivers of potential participants will be asked to provide verbal consent for the questions being asked in the phone script. The study staff completing the call will be required to destroy the information collected in the phone call if the participant decides they are not interested in the study. If the participant signs a consent form then the information will be kept in a locket cabinet and kept with study data. Justifications for these waivers:

- The recruitment procedures involve no more than minimal risk to the research subjects and their privacy because: the information we are collecting in this phone call does not surpass the probability and magnitude of harm or discomfort anticipated during a routine interview with a health care professional. Participants also have the option not to answer any questions they do not wish to answer.
- The waiver of HIPAA authorization and caregiver permission will not adversely affect the rights, including the right to privacy, nor adversely affect the welfare of the subjects whose data are being used because: the information will be safely destroyed if the participant does not wish to proceed with study procedures after the phone call. If the participant does wish to proceed with study procedures then the information collected during the phone call will be kept in a locked room, per HIPAA requirements.
- The research could not practicably be conducted without the waiver of consent and/or HIPAA Authorization because: This interview will take

place over the phone. It is impractical to collect a signature of consent since this phone call will only take about 15 minutes to complete.

- The research could not practicably be carried out without access to protected health information because the information is needed for additional contact of subjects who are interested in participating and the health information is needed to complete the screening procedures.

- *If the research involves a waiver the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations.*

Subjects who are not yet adults (infants, children, teenagers)

- Subjects will be enrolled between 6 and 8 years of age inclusive. Subject age will be confirmed with caregiver or legal guardian during the initial phone contact and again at time of consent.

  Caregiver permission will be obtained from one legal guardian. Only parents or legal guardians will be allowed to sign the consent (caregiver permission) form.

- *Caregiver permission will be obtained from:*

  One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

- *Indicate whether assent will be obtained from all, some, or none of the children. If assent will be obtained from some children, indicate which children will be required to assent.*

  Children who are 5-6 yo at time of enrollment will be asked to provide verbal assent (please see verbal assent script uploaded to Click). Children who are 7-10 yo at time of enrollment will be asked to sign an assent form.

- *When assent of children is obtained describe whether and how it will be documented.*

  We will keep signed assent forms (7-10 year old subjects) in a locked

cabinet at CHBD and their assent will be noted on in our participant tracking database. Children who provide verbal assent (5-6 year olds) will have their assent noted in the participant tracking database.

Cognitively Impaired Adults

N/A

Adults Unable to Consent

N/A

Consent for use of HUD

N/A

30.0 Process to Document Consent in Writing

We will be following "SOP: Written Documentation of Consent (HRP-091). Please see attached caregiver permission and teacher consent forms.

31.0 Drugs or Devices

N/A

32.0 Good Clinical Practice

We have committed to conduct the described study per International Center for Harmonization of Good Clinical Practice (ICH-GCP).