TITLE: FITT exercise counseling with interactive accelerometry and physical activity in adolescents at increased risk of early cardiovascular disease: A pilot study

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Boston Children's Hospital

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Part B: Experimental Design and Protocol – ALL APPLICANTS MUST COMPLETE THIS FORM

All investigators must submit a completed Part B with their New Protocol or Continuing Review application. If a protocol from a corporate sponsor or cooperative group is available, this must also be submitted.

Each question in Part B should be answered thoroughly with answers that are specific to how the research will be conducted at Children's Hospital, Boston.

Do not cut and paste from the protocol or from a grant application to complete Part B. Instead, complete each question in Part B by referencing the applicable page and section number of the protocol which answers the questions in Part B. For some questions in Part B, such as those regarding recruitment methods, confidentiality provisions, and adverse event reporting, you will need to provide complete answers rather than references to the protocol, since the protocol will not address these items as they apply specifically to how the research will be conducted at CHB.
Further information may be obtained by referring to the polices and procedures on the CCI website

Please provide a brief summary or abstract of this research protocol.

Background: Obesity is increasingly common in childhood and adolescence and is associated with high rates of abnormal cholesterol and high blood pressure, type 2 diabetes and cardiovascular disease. Studies suggest that regular physical activity can reduce cardiovascular risk factors in children. Despite evidence of its benefits, exercise training prescribed by physicians for overweight children is traditionally vague, developmentally inappropriate, and/or fraught with psychological barriers. There has been recent increased interest in the use of interactive new technologies to promote physical activity, prevent or reverse unhealthy weight and improve physical fitness in youth. **Objective**: To determine whether exercise counseling with BodyMedia, an online interactive accelerometer, has an effect on physical activity levels, fitness levels, and cardiometabolic measurements in pediatric patients with cardiovascular risk factors. **Design**: A randomized controlled pilot study of children at increased risk for atherosclerosis comparing exercise prescription combined with BodyMedia to a control group receiving physician counseling alone (standard of care). **Measures**: All study patients will be assessed at baseline and at the end of the study period directly for energy expenditure and physical activity using accelerometry; physical fitness will be assessed by standard VO2 stress at the same time periods. Available blood pressure and lipid levels will be gathered from clinical encounters, and self-efficacy will be evaluated by questionnaires. **Primary Hypothesis**: This interactive technology coupled with support from exercise specialists will increase the energy expenditure of our patients over standard of care provider counseling. **Secondary hypotheses**: There will be greater improvement in measured physical fitness, lipid profiles, blood pressure, arterial stiffness, BMI, BMI percentile, and self-efficacy in the intervention group compared to control.

1. Specific Aims /Objectives

Primary aim: This pilot study seeks to compare the change in energy expenditure and fitness levels of patients seen in the Children's Hospital Preventive Cardiology program receiving standard of care provider exercise counseling to similar patients receiving FITT (Frequency, Intensity, Time, Type) exercise prescription and counseling combined with BodyMedia supported by an online interactive tool.

- Our primary hypothesis is that this interactive technology coupled with support from a exercise specialist will increase the energy expenditure of our patients over standard of care provider counseling
- Secondary hypotheses include greater improvement in measured physical fitness, lipid profiles, blood pressure, arterial stiffness, BMI, BMI percentile, and self-efficacy in the intervention group compared to control.

2. Background and Significance

Obesity is increasingly common in childhood and adolescence, and is a major threat to health. Obese pediatric patients have high rates of abnormal cholesterol and high blood pressure (AHA 2010) and childhood obesity is predictive of type 2 diabetes and cardiovascular disease (CVD) (Morrison 2008). Studies suggest that regular physical activity can reduce cardiovascular risk factors in children. Exercise training can improve cardiovascular risk factors (Ferguson 1999) and the intra-individual clustering of cardiometabolic risk factors (Reinehr 2009), in individuals with obesity (Klijn 2007) and diabetes (Caranti 2007). Reduction in risk factors may occur both by direct effects (e.g. blood pressure reduction, increasing HDL), and indirectly through weight reduction. National guidelines recommend that children accumulate at least 60 minutes per day of moderate to vigorous physical activity on most days of the week (CDC 2010), based on evidence of physiologic benefits (Strong 2005). However, most children are not meeting these recommendations; declining levels of physical fitness among children and adolescents contribute to the obesity-associated health risks of future generations (American Heart Association, 2005).

Despite evidence of its benefits, the recommendation for physical activity from physicians given to overweight children is traditionally vague, developmentally inappropriate, and/or fraught with psychological barriers. Standard recommendations, even if delivered by pediatric providers, may not be supported by sufficient motivational assistance and are given at such infrequent interactions as to be minimally helpful. Recently there has been increased interest in the use of interactive new technologies to promote physical activity, prevent or reverse unhealthy weight, and improve physical fitness in youth (Whiteley 2007; An (in press)). These technologies have the potential to allow for remote patient monitoring that may offer more reliable assessments of the patients' progress, better accessibility, improved patient comfort and compliance as well as decreased cost both for patients and the health-care system. Studies in adults support the efficacy of both self-monitoring and frequent contact in supporting behavior change; in adults interactive technologies can intensify anti-smoking attitudes, improve prevention behaviors, influence dietary habits, increase physical activity, strengthen adherence to medical treatment plans, and improve chronic disease self-management (Norman 2007).

BodyMedia (http://www.bodymedia.com) is a relatively new technology that incorporates accelerometry, temperature, moisture evaporation (reflecting sweat), and heart rate into algorithms designed to assess energy expenditure. Validation studies demonstrate both reproducibility and validity in adults, comparing energy expenditure estimates to indirect calorimetry (correlation coefficient of 0.89, Andre 2006) and in children (correlation coefficient of 0.86 for treadmill and exercise bike, and at rest). Dorminy et al (2005) tested this technology in African-American children, demonstrating correlations with indirect calorimetry of 0.91 for exercise and 0.984 for rest, when adjusted for body weight. Other studies have reported similar results (Calabro 2009).

BodyMedia has been used as a behavioral support for weight loss in two adult studies (Sui et al, presented at AHA EPI/NPAM joint conference 2010), with double the weight loss seen in the BodyMedia group compared to either a more conventional group-based weight loss program or self-directed weight loss. A second protocol tested intermittent vs. continuous BodyMedia use, also demonstrating double the weight loss in patients using the BodyMedia continuously for 12 weeks compared to intermittent use (Polzien 2007). There are no reports of using BodyMedia technology as a behavioral support for weight loss or increasing physical activity.

Interventional studies indicate that delivering exercise counseling using the specific guidelines of frequency, intensity, time, and type of exercise (FITT) have shown beneficial changes in the skeletal health, aerobic fitness, and muscular strength and endurance of youth. Using this approach of delivering exercise counseling to achieve national recommended guidelines has proven to be a successful health promotion and disease prevention strategy (Strong 2005).

Pulse wave velocity (PWV) testing is a method of measuring arterial stiffness non-invasively. Atherosclerotic events, such as myocardial infarction or stroke, and chronic CVD like heart failure, are associated with arterial stiffness, independent of classic and newer cardiovascular risk factors. In fact, some data suggests that compared to commonly measured CVD risk factors, arterial stiffness is the best independent predictor of CVD events in adults (Mitchell 2010). Applanation tonometry has emerged as the gold standard technology for noninvasive, high volume measurement and decomposition of pulsatile arterial load, especially with respect to arterial pressure waveform analysis and PWV. A recent policy statement from the AHA states, "increasing experience in pediatric patients suggests that the evaluation of arterial stiffness parameters in youth is not only reproducible and valid but also important. Although no true gold standard for local or regional in vivo measurement of arterial stiffness has been established, PWV has become the most widely studied, reproducible, accepted, and utilized method. With the limited available data in pediatric populations, more studies, including those of a longitudinal design, are required" (Urbina 2009).

3. Preliminary Studies/Progress Report

1. We assessed the impact of an exercise prescription program upon the exercise capacity of adults with CHD. 18 patients aged 37±13 years with a variety of CHD's underwent an initial cardiopulmonary exercise test (CPET) and were then provided with a prescription for a self-administered exercise program. Subjects were divided into "compliant" and "non-compliant" groups on the basis of their responses to questions administered at the time of the follow-up CPET. Peak VO_2 averaged 19.0±7.1 ml/kg/min on the initial CPET and 19.4±7.2 on the follow-up CPET (p=NS). Those that were "compliant" increased their peak VO_2 from 20.1±9.3 to 21.5±9.1 ml/kg/min (p=0.025). In contrast, the peak VO_2 of the non-compliant group decreased from 17.7±3.2 to 17.1±3.3 ml/kg/min (p=NS). Improvements in peak VO_2 of at least 1.0 ml/kg/min were observed in 7/9 compliant patients and in only 1/8 non-compliant patients ($p<0.02$). Compliant patients also achieved an average weight loss of 0.58±3.8 kg, whereas non-compliant patients gained an average of 0.65±1.8 kg. We concluded that when adults with CHD adhere to an exercise prescription, improvements in peak VO_2 are often achieved and successful weight loss is sometimes realized. However; poor compliance with exercise prescriptions was common, and limited the effectiveness of this therapeutic intervention.

2. We reviewed our clinical experience with FITT exercise prescription (Frequency, Intensity, Time, Type) and counseling combined with monthly motivational and educational follow-up contact in the form of mailings, e-mails, and phone calls affects physical activity as measured by self-report (METS). When available, we examined changes in physical fitness (VO2 max), attitudes and self-efficacy regarding physical activity, BMI z-score, and cardiovascular risk factors.

Forty patients with hyperlipidemia, overweight/obesity and/or HTN received FITT counseling in addition to standard care counseling by physicians during their visit in the Preventive Cardiology Clinic. Subjects were divided into "compliant" and "non-compliant" groups on the basis of information gleaned from their follow up clinic visit notes. Those that were compliant showed improvement in their lipid profile, BMI and physical activity levels. In contrast, non-compliant patients either showed no change or worsened cardiovascular risk factors. We concluded that when children with cardiovascular risk factors adhere to an exercise prescription, improvements are often achieved, and successful weight loss is sometimes realized. Unfortunately, poor compliance with exercise prescriptions was again common, and limited the effectiveness of this therapeutic intervention.

4. Design and Methods

a. Study Design

A randomized controlled pilot study comparing exercise prescription based on the FITT principle combined with BodyMedia, an online supported accelerometer, to a control group receiving physician counseling alone (standard of care). All participants will wear an accelerometer to measure physical activity for one week at the start of the intervention. At the end of that week, patients who have worn the accelerometer for more than 8 hours per day for at least 3 days will be randomly assigned to either FITT

counseling by a pediatric exercise physiologist + interactive accelerometer, or office provider counseling (standard of care). The intervention group will be asked to continue to wear the accelerometer everyday (most waking hours) and log their activity by regularly (3 times a week) uploading the device for a period of 3 months, use of the internet must be supervised by a parent or guardian. Their activity will be monitored via the online site on a regular basis by study personnel and feedback will be provided at least once a week through email and/or phone calls. At the end of the intervention all participants will be asked to again wear the accelerometer for 1 week to assess physical activity, and complete questionnaires assessing attitudes towards and self-efficacy around physical activity. Lipid levels and blood pressures, when obtained for clinical visits in Preventive Cardiology Clinic, will be evaluated for change over the course of the intervention. Participants will be given a non-invasive pulse wave velocity test. Pulse wave velocity testing is a painless non-invasive test to evaluate the time it takes for blood to move from the heart to the rest of the body. In practice, this involves using a fingertip probe placed lightly on the brachial artery – the internal aspect of the elbow, the carotid artery – side of the neck, and the femoral artery – groin area. This final measurement is easily performed through light clothing. In order to coordinate the timing of the pulse wave, four EKG electrodes are placed on the patient. The entire procedure takes about 15 minutes in experienced hands. There is no risk involved in this non-invasive procedure. It is less painful than a blood pressure measurement.
The research study will require 2 visits to the Preventative Cardiology Clinic in Boston or Waltham, based on their preference. Each visit may take up to 1-1.5hours.

b. Patient Selection and Inclusion/Exclusion Criteria

A sample of 60 patients at increased risk for atherosclerosis will be recruited from Preventive Cardiology.

Inclusion criteria:
Subjects will be eligible for enrollment based on the following criteria:
1) Patients at increased risk of atherosclerosis based on lipid profiles (TC > 199 mg/dL, HDL < 40 mg/dL, LDL > 129 mg/dL, blood pressure (SBP or DBP > 90th percentile), obesity (>85%BMI)
2) Ages 13-21 years
3) Reporting an average of less than 60 minutes per day of moderate to vigorous exercise most (5) days of the week.
4) Regular access to the internet with the capacity to download the device
5) Commitment on the part of a parent to supervise internet access as part of this protocol

Exclusion criteria:
1) Unable to exercise based on physician recommendations or medical conditions
2) Unable/unwilling to complete requirements of the research study including consent and assent.
3) Not proficient in English

c. Recruitment Methods

i. HOW, WHERE and WHEN will potential subjects be recruited?

Patients will be screened for potential participation based on previous Preventive Cardiology clinic visit notes. If the child appears to meet the eligibility criteria for the study, a recruitment letter and opt-out postcard will be sent with a pre-clinic mailing at least 2 weeks prior to the scheduled visit. If patients indicate non-participation preference by returning the postcard, they will not be contacted about the study. If the postcard is not returned, study personnel will approach the patient during their clinic visit to discuss participation, eligibility and exercise habits. In addition, we will approach patients in the Lipid Clinic in Boston and Waltham that did not receive a mailing, but are potentially eligible for the study. If eligible we will obtain consent for enrollment into the study. A study visit will be scheduled during the initial clinic visit. The research study will require 2 visits to the Preventative Cardiology Clinic in Boston

or Waltham, based on participate preference. Each visit may take up to 1.5 hours. A gift card or cash incentive of $15.00 will be given to the patient when they qualify and arrive at their first study visit. If patient requires more time to think about the study and request a phone call follow up, a study staff member will contact them via phone to discuss study participation. Phone calls will only be made if the patient has requested to be contacted at a later time and expressed interest in the study. If potential participant decides they would like to enroll in the study, verbal consent will be obtained and the device will be mailed to patient. Written consent will be obtained during the first study visit. Patients that are not interested in the study at the time of their clinic visit will be tracked in a spreadsheet and will not be contacted again.

ii. WHAT recruitment methods and materials (e.g. posters, fliers) will be used? - *attach all materials*

Methods of recruitment will include letters and a brochure.

iii. WHO will be responsible for subject recruitment?

Providers from the Preventative Cardiology Program including MDs, RNs and PNPs and Exercise Physiologists, Lead EKG Technician, Research Fellow, and Research Assistant from Children's Hospital Cardiovascular Clinic will recruit subjects by phone, mail, and clinic visit.

Main Study Consent (during Clinic Visit): Participants will be asked to provide informed consent/assent during their clinic visit.

d. Description of Study Treatments or Exposures/Predictors

Treatment for the study involves randomizing participants into FITT exercise counseling in conjunction with an interactive accelerometry tool (intervention) and physician counseling alone (standard of care/control) The FITT principle is based on standard exercise prescription guidelines supported by the American College of Sports Medicine (ACSM). FITT stands for Frequency – the number of days per week one exercises, Intensity – how hard one exercises, Type – aerobic vs. non aerobic exercises, Time – the duration of the exercise session. The ACSM combined with the Center for Disease Control and Prevention (CDC) recommendations for aerobic activities for children and adolescents should do 60 minutes or more of physical activity daily. Activities should consist of aerobic type exercises, most of the 60 minutes or more per day should be moderate or vigorous intensity. Vigorous intensity should be at least 3 days per week. Muscle strengthening physical activities and bone strengthening activities should be incorporated at least 3 days per week as part of the 60 or more minutes. Patients will be counseled on this principle and each participant will receive a personal exercise prescription based on the FITT principle, as well as monthly phone follow-up.

Participates who engage in FITT exercise counseling in conjunction with accelerometery will also receive a BodyMedia arm band with an online subscription. BodyMedia FIT is a weight management system consisting of the BodyMedia Armband monitor and an online Activity Manager. The BodyMedia FIT Armband estimates the calories burned during your daily activities based on heart rate, perspiration, movement in space — from working out to doing homework; additionally, BodyMedia monitors the quality of sleep, an important factor in weight loss. The information tracked can easily be managed with BodyMedia's online Activity Manager. Patients have the ability to add in a food log, a feature that could improve weight loss by virtue of the logging function. Patients will just plug the unit into their computer's USB port each day to automatically upload info; the device stores up to 14 days of data, a feature that allows a little bit of flexibility for a busy team. Participants can simply log the food they ate via the computer. The activity Manager tool gives the patient and research team a running report of progress toward their goals, including steps taken, time spent in moderate and vigorous activity, nutritional

analysis and sleep efficiency, including any personal bests. The research team will review patient's data on a weekly basis and discuss the findings via phone or email to promote patient compliance and answer any questions or concerns they may have.

Participants that do not receive intervention will be provided a personalized FITT exercise counseling session following the study.

e. Definition of Primary and Secondary Outcomes/Endpoints

Measurements:

Accelerometry and Energy Expenditure: BodyMedia Armband technology incorporates accelerometery, temperature, moisture evaporation (reflecting sweat) and heart rate into algorithms designed to assess energy expenditure.

Arterial Stiffness: Pulse wave velocity is a measure of the speed of transit of the pulse generally measured from the carotid to the femoral artery using ECG gated measurements of the peak pulse impulse. NIHem Hemodynamic Acquisition system quantifies pulse wave velocity (PWV), as well as other measures of arterial hemodynamics. Carotid- femoral pulse wave velocity has emerged as the "gold standard" index of aortic stiffness. The NIHem system has been previously validated to resolve pulse wave analysis in time or frequency domains and has been used extensively in the NIH/ NHLBI's Framingham Heart Study to at more than 12,000 participant visits with 90% reproducibility. Median time to complete a full set of measurements is roughly 15 minutes.

Questionnaires: A pre and post exercise questionnaire, adapted from the Youth Risk Behavior Survey and from the Trial of Activity for Adolescent Girls (Dishman 2009) will be administered. Questions will assess self efficacy, social support, perceived barriers and enjoyment related to exercise.

Laboratory testing: All study subjects will undergo testing including a fasting lipid profile consisting of TC, HDL, low-density lipoprotein (LDL), and triglycerides (TG) concentrations. Additional labs that will be collected, if available, include liver transaminase alanine aminotransferase (ALT), C-reactive protein (CRP), a relatively stable measure of the inflammatory state known to be associated with cardiovascular risk in adults, glycosylated hemoglobin (Hgn A1C) to assess long term glucose homeostasis. Fasting insulin and glucose will also be collected, if performed for clinical reasons by Preventive Cardiology or the patient's primary care.

Height, Weight, and Blood Pressure measurements will be obtained according to clinical practice guidelines. Blood pressure will be measured in a standardized manner in the right arm after 5 minutes of quiet sitting by automatic blood pressure device. One measurement of height (nearest 0.1 cm) and weight (nearest 0.1 kg) will be obtained. Body mass index (calculated as weight/height ^{2} [kg/m^2] using CHB EMR/PowerChart) will be used to estimate excess overall adiposity. Additional measures of auscultative blood pressure will be collected if available. Dr. De Ferranti will interpret the anthropometric data.

f. Data Collection Methods, Assessments and Schedule (what assessments performed, how often)

Patients enrolled in the study will be informed that the research data collection will add about an hour to their current clinical visit. However, patients will gain information about their exercise capacity.

Table 1 Data Collection Schedule

Measures	Baseline visit	12-week visit	Minutes
Height, weight, blood pressure	X	X	10
Arterial Stiffness	X	X	20
Fasting lipids, glucose, insulin, HgnA1C, CRP, ALT	X	X	20
Accelerometry	X	X	10
Questionnaires	X	X	20
Chart Review for Medical History	X	X	20
Study Total			100

g. Study Timeline (as applicable)

See Table 2. Study recruitment will start in April of 2011and continue until target enrollment is reached or funding is exhausted.

Table 2 Study Timeline (2011)

Study Event	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar
Recruitment		X	X	X	X	X	X	X	X	X			
Consent/ Baseline		X	X	X	X	X	X	X	X	X			
Patient Follow-up		X	X	X	X	X	X	X	X	X			
12-Week Assessment					X	X	X	X	X	X	X	X	X

h. Adverse Event Criteria and Reporting Procedures

Adverse events are not anticipated as part of this intervention based on the nature of the activity involved. Serious events requiring medical attention will be reported immediately to Drs. de Ferranti and Rhodes as well as to CCI per the reporting policy.

i. <u>If the Investigator is the Sponsor/Assignee (IND or IDE-holder)</u>, he/she is responsible for selecting a qualified monitor who will monitor the progress of all clinical investigations conducted under the IND or IDE. Please describe the monitoring plan for this protocol below:

↳ Note: the EQuIP office provides monitoring services and advice. For info, contact EQuIP @ 5-7052.

☒ Not applicable

5. Data Management and Statistical Analysis

Data Management Methods

Data will be collected by study personnel including exercise physiologist, research fellow, head EKG technician and exercise student intern. The research team will assure that all data is collected. The data will be recorded in a de-identified manner using study IDs only. The key between participants and study IDs will be stored in a password protected electronic file. The data will be entered using a standard data management program (REDCap) on an ongoing basis. The data will be examined systematically for quality control and data cleaning purposes during the course of the study and again at the end. A portion of the data forms will be double entered for quality assurance purposes. The assistance of the Clinical Research Program will be solicited for technical support in these areas.

b. Quality Control Method The data will be examined systematically for quality control and data cleaning purposes quarterly during the course of the study and again at the study end prior to analysis.

c. Data Analysis Plan

The primary test of hypothesis is the comparison of change in Energy Expenditure (ΔEE) between baseline and final visit (12 weeks) in children receiving FITT Counseling plus BodyMedia as compared to children receiving physician counseling alone (standard of care/control). A two sample t-test will be used for this comparison. In the event of non-normality, the Wilcoxon rank sum test will be used. Secondary outcomes will be analyzed similarly. Linear regression will be used to adjust for any suspected confounding. In all tests, a two tailed p-value <0.05 will be considered statistically significant.

d. Study sample size and power considerations. . A total sample size of 40 (20/group) would provide adequate power to detect differences in physical activity counts as small as 0.9 standard deviations. Based on previous studies and clinical experience we expect ≤ 30% attrition rate over 6 months: 30 patients per study group will be enrolled to ensure ≥20 per group complete the study

e. Study Organization

The study group will meet monthly to review progress and results of the study. Dr. de Ferranti and Dr. Rhodes will review testing results as they are received. The Clinical Research Team will oversee recruitment and study activities for the Study.

f. Data and Safety Monitoring Plan

The physical activity recommendations given as part of this protocol are based on national guidelines, modified for the individual based on exercise testing data. Physical activity is generally recommended for obese children and adolescents. The study does not employ pharmacological agents or notably invasive procedures. Thus, this study poses minimal risk to subjects. For this reason, the data and safety monitoring plan (DSMP) will focus on 1), 2) injury issues related to initiating new physical activities, 3) web-based communications, and 4) enrollment and drop-out rates. Subjects will be closely monitored by the study team. Serious adverse events will be promptly reported to the funding group and the Institutional Review Boards (IRB) of Children's Hospital Boston.

The frequency of data review is summarized in Table 3. The study director will be responsible for assembling the data and producing summary reports for review by the Research Team and the DSMB.

Table 3

Data type	Frequency of review
Subject accrual	Monthly
Drop-out rate	Monthly
Data collection and completion	Quarterly
Adverse events (injuries)	Quarterly
BodyMedia Online Activity Manager	Weekly

- Clinical Data: If significant medical conditions are discovered as part of the research protocol, participants and primary care physicians will be notified by phone and by mail, as appropriate, and referral for evaluation or treatment will occur in consultation with the primary care physician.
- Subject accrual, Drop-out rate. Review of the rate of subject accrual and adherence to inclusion/exclusion criteria will occur monthly during the recruitment phase. Drop-out rate will be monitored on a monthly basis.

- Adverse events. In view of the nature of the intervention, we do not expect significant adverse events to occur as a result of the study. Nevertheless, all adverse events will be evaluated by the PI and the mentor within 72 hours (minor or moderate) or 24 hours (serious or fatal), and reported to the IRB of Children's Hospital according to hospital policy. A case report form will be used to monitor adverse events.
- Overall progress of study. The PI will review the safety and progress of this study on a monthly basis. She will also review all data collection forms on a quarterly basis for completeness and accuracy of the data, as well as protocol compliance. The research team will have access to the participant's BodyMedia online activity manager and will observe and intervene with patient.

6. Risks and Discomforts

The study has been designed to minimize risks and discomforts. Questions about medical and family history, diet and exercise may be distressing for some participants. Referrals to the appropriate professionals will be made available as necessary and on request. However, the participating adolescents have known cardiovascular risk factors that require intervention of some type, and exercise would be indicated for these children. This study has been designed to keep risks to the lowest level possible. A physician will be available on a 24-hr per day basis should any problems arise.

Exercise counseling through the web-based tool will be performed by members of the study team. Any concerns raised as part of this communication will be reviewed every 2 weeks or more frequently as necessary by the study team. Initial consultation with Dr. David Demaso, Chief of Psychiatry, or his designate, and with media experts in the Children's Hospital Boston community will be sought prior to the initiation of the protocol to learn from their extensive experience with web-based and internet patient communications.

Data collection will be reviewed regularly for clinically significant abnormalities, and every month by the research team to ensure data collection is proceeding accurately and completely. Results of all clinically relevant tests and procedures will be provided to the parent or guardian of each participant along with an explanation of the results and instructions to contact the child's the primary care physician for appropriate follow-up of abnormal values. Abnormal findings will also be communicated to the participant's primary care physician directly, should the participant authorize this.

Risk of injury will be discussed prior to the exercise program and will be reviewed on a weekly basis to prevent injury from occurring. Muscle soreness is a common discomfort experienced with exercise in the beginner, however not life threatening.

7. Potential Benefits

The potential benefits from participating in this project include possible improvement of cardiovascular risk factors related to increased physical activity. Compensation to families for their time will be provided by way of parking expenses reimbursed, 10.00 gift card or cash incentive when qualifying and arriving for first study visit, and a $50.00 gift certificate to the subject that has successfully completed the study.

8. Privacy Provisions

Only the minimum amount of information necessary to complete the research study will be collected to maintain individuals' privacy. All participants will have access to their own medical information, as appropriate to the intervention. Medical information will only become part of the participant's medical record if the information is determined pertinent to the care that s/he receives at Children's.

9. Confidentiality Provisions

Data will be collected and stored in a de-identified manner aside from a study ID log and contact information file, which will be maintained separately from general information and under protection

accessible only to study personnel. Data will be reported in the aggregate. The consent form will clearly describe potential confidentiality risks. Only study personnel will have access to the study ID log which links study ID to identifiers.

10. References

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Ethnic Cohort of Middle-School Girls: Two-year Prospective Study. *Journal of Pediatric Psychology* pp. 1–11, 2009

11. Appendix Materials – please check off as appropriate if included with submission.

- ☐ Sponsor's Protocol
- ☐ Investigator brochure (3 copies)
- ☐ Flow charts, schemas
- ☐ Other
- ☐ Federal grant application (3 copies)
- ☒ Survey, questionnaires, assessments
- ☒ Recruitment letters, postings, flyers
- ☒ Materials given to subjects (reminders, letters, thank-you, etc.)*

** see instructions for further information*