Congenital Heart Disease Physical Activity Lifestyle Study (CHD-PALS)

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Version 7

30 April 2021

STATEMENT OF COMPLIANCE

The study will be carried out in accordance with Good Clinical Practice (GCP) as required by the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46; 21 CFR Part 50, 21 CFR Part 56, and 21 CFR Part 312)
- ICH E6; 62 Federal Register 25691 (1997)
- NIH Clinical Terms of Award

All key personnel (all individuals responsible for the design and conduct of this study) have completed Human Subjects Protection Training.

SIGNATURE PAGE

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations.

Site Investigator:*

Signed: _____ Date: 10/29/2019

Name
Title

** The protocol should be signed by the local investigator who is responsible for the study implementation at his/her specific site.*

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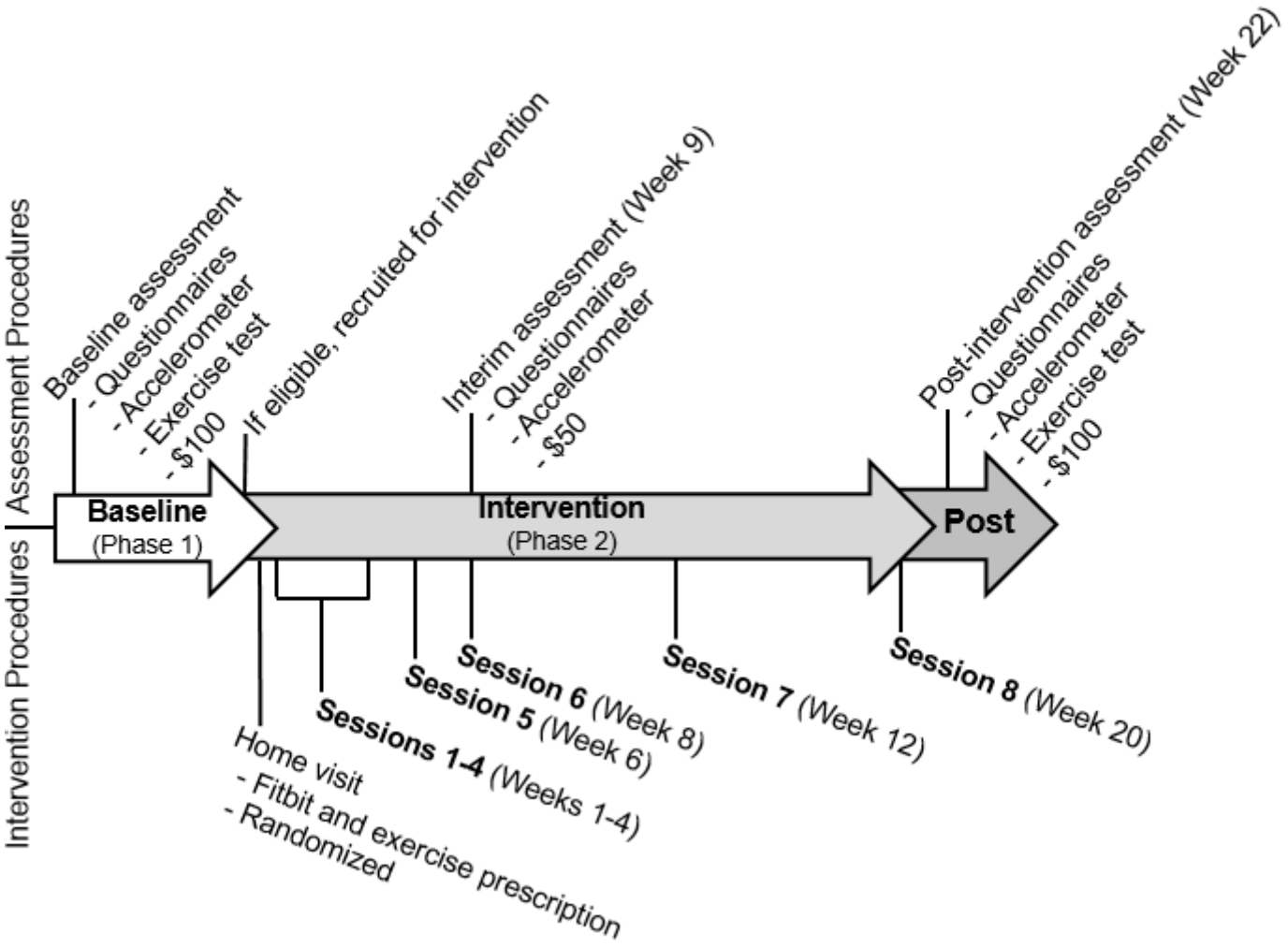
LIST OF ABBREVIATIONS

AHA	American Heart Association
IPAQ	International Physical Activity Questionnaire
IRB	Institutional Review Board
CHD	Congenital Heart Disease
CHD-PALS	Congenital Heart Disease Physical Activity Lifestyle Study
CITI	Collaborative Institutional Training Initiative
CO-I	Co-Investigator
DSMB	Data Safety Monitoring Board
Mplus	Statistical Modeling Program
MVPA	Moderate to Vigorous Physical Activity
NCH	Nationwide Children's Hospital
PA	Physical Activity
PI	Principal Investigator
PROMIS	Patient-Reported Outcomes Measurement Information System
SB	Sedentary Behavior
RCT	Randomized Control Trial
REDCap	Research Electronic Data Capture
VO_{2max}	Peak Oxygen Uptake

PROTOCOL SUMMARY

Title:	**Congenital Heart Disease Physical Activity Lifestyle Study (CHD-PALS)**
Abstract:	Over 40,000 infants are born in the U.S. with congenital heart disease (CHD) each year, and with advancements in medicine, more than 90% of these individuals now live well into adulthood. This growing, and aging, population of CHD survivors is at risk for developing cardiac-related complications such as coronary disease, heart failure, and hypertension, which fortunately are responsive to lifestyle change. An American Heart Association (AHA) Scientific Statement highlights the important health benefits gained from increasing physical activity (PA) among children and adults with CHD, noting research evidence of better vascular health, reductions in hypertension, and lower rates of obesity. Despite this, evidence suggests that CHD survivors are less active than healthy controls, placing them at an elevated risk for preventable morbidity and premature mortality. Therefore, the current study adapts a PA lifestyle intervention to young adult CHD survivors (ages 18 – 25) who have moderate to complex CHD with the goal of increasing MVPA and decreasing SB. The study is split into 2 phases; a total of up to 90 young adults will participate in Phase 1 to determine participants' eligibility for Phase 2. Phase 2 is the randomized control trial in which a total of 40 young adults are randomized to either the comparison arm (Fitbit and exercise prescription) or the intervention arm (Fitbit, exercise prescription, AND videoconferencing sessions with a coach).
Population:	Participants: For Phase 1 we aim to recruit up to 90 young adults (ages 18 – 25 at enrollment) who have moderate to complex CHD. For Phase 2 we aim to recruit 40 young adults (~17 per arm).
Study Duration:	2 years (2019-2021)
Participation Duration:	Phase 1: 2 weeks Phase 2: 22 weeks
Description of the Intervention:	Phase 2 of the study consists of being randomized into one of two arms; the comparison arm receives a Fitbit and an exercise prescription based on the results of the Phase 1 stress test. The intervention arm receives a Fitbit, an exercise prescription, and 8 videoconferencing sessions with a PA coach,

	which takes place over 20 weeks. Each session lasts 20-30 minutes and focuses on changing attitudes, perceptions of social norms, and perceptions of control over for engaging in PA, based on the principles of the Theory of Planned Behavior.
Objectives:	The long-term goal of this research study is to establish an effective intervention for sustaining increased levels of MVPA that will reduce morbidity and healthcare costs for CHD survivors. The objective of this study is to adapt a lifestyle PA intervention to young adult CHD survivors at greater risk for future morbidity due to having more complex disease. This will involve (1) evaluating the feasibility of the intervention and (2) obtaining qualitative feedback from participants on the content of the intervention sessions and study procedures using focus groups. We hypothesize that young adults will rate participating in as enjoyable, easy, relevant, and useful. Additionally, qualitative data about participants' study experiences will inform modifications to the session content and study procedures for the larger trial. The *rationale* for the proposed research is to obtain pilot data that will shape the next phase of investigation: determining the efficacy of this intervention for sustaining increased PA among young adult CHD survivors. Ultimately, we hope that knowledge gained from this line of research will extend longevity and optimize quality of life for CHD survivors as they age further into adulthood.
Description of Study Design:	Randomized controlled trial with two treatment arms: (1) Comparison arm: Fitbit, exercise prescription and (2) Intervention arm: Fitbit, exercise prescription, and 8 videoconferencing sessions with a PA coach over the course of 20 weeks.
Estimated Time to Complete Enrollment (n=90):	2 years


Assessment Procedures
Intervention Procedures
Baseline assessment
- Questionnaires
- Accelerometer
- Exercise test
- $100
If eligible, recruited for intervention
Interim assessment (Week 9)
- Questionnaires
- Accelerometer
- $50
Post-intervention assessment (Week 22)
- Questionnaires
- Accelerometer
- Exercise test
- $100
Baseline
(Phase 1)
Intervention
(Phase 2)
Post
Home visit
- Fitbit and exercise prescription
- Randomized
Sessions 1-4 (Weeks 1-4)
Session 5 (Week 6)
Session 6 (Week 8)
Session 7 (Week 12)
Session 8 (Week 20)

1 KEY ROLES

Individuals:

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2 BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

2.1 Background Information

Congenital heart disease (CHD) comorbidities and cost

Over 40,000 infants are born in the U.S. with CHD each year, and with advancements in medicine, more than 90% of these individuals now live well into adulthood.[1-3] This growing, and aging, population of CHD survivors are at risk for developing cardiac-related complications such as coronary disease, heart failure and hypertension, which fortunately are responsive to lifestyle changes,[4] such as increasing PA and decreasing sedentary behavior. Those with moderate and complex cardiac lesions[4] are the ones in greatest need for intervention, as evidenced by significantly higher premature mortality rates as compared to the general population due to underlying cardiovascular issues.[5] Increased rates of hospitalizations costing more than $3.16 billion annually due to higher incidence of coronary artery disease and heart failure among CHD survivors can be mitigated by early lifestyle intervention.[6]

Physical activity (PA) engagement and benefits

An American Heart Association (AHA) Scientific Statement[7] highlights the important health benefits gained from increasing PA among children and adults with CHD, noting research evidence of better vascular health, reductions in hypertension and lower rates of obesity. In fact, newly published guidelines for the management of adults with CHD encourage the counseling of adult CHD survivors on PA for both prevention and treatment of comorbidities that increase risk for premature mortality.[8] Positive health behaviors often decline during adolescence and young adulthood, and CHD survivors are no exception, which may lead to poor health behaviors later in adulthood.[9-12] Young adulthood (18-25 years old) is a unique developmental stage hallmarked by instability (e.g., romantic relationships and job changes), as well as greater focus on qualities of character, such as accepting responsibility for one's self.[13] Heightened risk behaviors identified during young adulthood may be due to identity exploration during this developmental period,[13] which may contribute to poorer disease self-management. For CHD survivors, this developmental period is also characterized by increased likelihood for lapses in care and/or loss to follow-up,[14,15] transfer of care to an adult medical setting, and assuming greater responsibility for managing one's disease. In the U.S., PA steadily declines during young adulthood before stabilizing in middle adulthood.[16] Furthermore, sex differences have been identified, such that males are more likely to report sustained PA during adulthood than females.[16] Given the enhanced focus on responsibility for one's

self and their future, young adulthood is an optimal developmental stage during which to conduct a health behavior lifestyle intervention.

Sedentary behavior (SB) is a risk factor

In addition to promoting moderate to vigorous physical activity (MVPA), a scientific statement by the AHA[7] also noted the importance of decreasing SB. Emerging evidence has identified inactivity as an equally important independent risk factor for cardiovascular complications, even when guidelines for PA are met. Among healthy children, SB increases by approximately 30 minutes per year from childhood into adolescence due to more time spent watching TV and/or using computers.[17] A similar pattern of increased SB over time has been identified in children and adolescents with CHD.[18] Time spent in SB among young adult CHD survivors via an objective measure of PA has only been documented by 1 study of 15 participants in Canada, which reported approximately 9.5 hours of SB/day.[19] Longitudinal research in the general population has identified increased time spent on the computer from adolescence to young adulthood, which may be an important contributor to greater SB in this age group.[20] Therefore, SB may be an equally important target for a lifestyle intervention. Consequently, in addition to measuring MVPA the current study will also measure SB, as a secondary outcome, due to the evidence of poor health outcomes with a predominantly sedentary lifestyle.

Physical Activity interventions and the Theory of Planned Behavior

PA interventions among CHD survivors have primarily focused on structured exercise programs, often using a cardiac rehabilitation model (3 days/week for 12 weeks). A systematic review of exercise training programs among children and young adults with CHD indicated that exercise training was safe and improved fitness levels, including among those with complex cardiac lesions, but the long-term sustainability is relatively unknown.[21] Of the 4 studies reviewed that included long-term follow-up, only 1 found a sustained effect, which was up to 5 years post-training. Of the other 3 studies, 1 did not find sustained effects and 2 only included survivors referred for cardiac rehabilitation, which limits applicability since many with CHD are never referred for cardiac rehabilitation. Interventions aimed at modifying lifestyle behaviors attempt to change long-term behavior by creating new positive habits rather than emphasize adherence to a time-limited structured program. The Theory of Planned Behavior[22] has been used as a framework for lifestyle interventions, including among individuals with heart failure[23-25] and rural populations with multiple cardiovascular risk factors.[26] The Theory of Planned Behavior contains 3 primary elements hypothesized to contribute to behavior change: attitudes about the behavior, subjective norms and perceived control. Interventions using this theory aim to address knowledge deficiencies and negative perceptions of the behavior (attitude), increase perception of others' approval of the behavior, such as family members, peers and medical staff (subjective norm), as well as trouble-

shoot barriers while increasing efficacy (perceived control). This framework may be particularly useful for CHD survivors since low PA in this population has been attributed to inaccurate negative attitudes about the consequences of PA on the heart or need for activity restriction by caregivers and others (e.g., sports coaches) during childhood.[27,28] Furthermore, poorer self-efficacy has been associated with lower levels of PA, as measured via accelerometer, among adults with CHD,[29] suggesting that targeting self-efficacy may positively influence PA engagement.

Objective measures to assess physical activity (PA)

Studies reporting MVPA in adults with CHD using accelerometry, the gold standard for measuring PA, are limited and none have emerged from the U.S. Dua et al. (2007) documented that among young adult (age 31.7±11.0) CHD survivors in the United Kingdom, only 23% who reported no functional impairments met national guidelines of at least 30 min/day of moderate intensity PA.[30] Sandberg et al. (2016) found that only 50% of Swedish adult CHD survivors (age was undefined) met the World Health Organization's recommendations for PA, which was true for both CHD survivors and age- and sex-matched controls.[31] McKillop et al. (2018) reported similar averages for min spent in MVPA, as did Dua and colleagues (26 min) on a small Canadian sample of 15 young adults.[19]Only 21% of U.S. adults from the general population meet the Centers for Disease Control and Prevention guidelines of at least 150 min/week of moderate intensity aerobic activity.[32] This suggests that a large portion of adult CHD survivors in the U.S. are also likely to be relatively inactive, despite being at greater risk for poor health outcomes.

These studies also draw attention to the need for using objective measures of PA to inform interventions, including using time spent in MVPA, as assessed by an accelerometer, for inclusion criteria so that young adults in need of intervention are targeted. In the current study, objective measures of MVPA will also be used to stratify random assignment of participants, as well as included as covariates in study analyses, thereby improving scientific rigor as compared to previous studies. This strategy will allow the detection of group differences with fewer participants and is in accordance with guidelines for clinical trials.[33] The current study will also examine change in peak oxygen uptake (VO_{2max}), a measure of exercise tolerance, as a secondary outcome. VO_{2max} has been identified as an independent predictor of 5-year mortality in young adult CHD survivors.[34] While change in VO_{2max} has been commonly assessed as an outcome in cardiac rehabilitation-style exercise interventions for CHD survivors, increased MVPA may not result in improved cardiorespiratory fitness. Current guidelines indicate that increasing moderate PA has significant health benefits, even in the absence of change in VO_{2max}.

Utilizing technology to facilitate behavior change: Videoconferencing and a popular activity tracker (Fitbit®)

Videoconferencing behavioral interventions have demonstrated feasibility among adults at risk for cardiovascular disease.[35] Videoconferencing as a mode of delivery for behavioral interventions has multiple advantages, such as eliminating some barriers to receiving the intervention (e.g., transportation, distance) and reducing costs for both providers and patients. Furthermore, videoconferencing and other modes of telehealth delivery have been shown to result in comparable rapport-building between youth and clinicians as face-to-face interventions and are accepted by families.[36] A Fitbit will be used in the current study as part of the intervention so that participants receive moment-to-moment feedback on their PA. Commercially available activity trackers, such as Fitbit, are popular and have been shown to align well with Health Behavior Theories because they offer immediate feedback and have tailored goal-setting functions.[37] Fitbits have been used with adolescents to track sleep,[38,39] and PA[40] in children with complex CHD as well as in interventions to increase PA levels among young adults with other chronic illnesses.[41,42]

2.2 Rationale

If young adults with moderate to complex forms of CHD demonstrate preliminary evidence of benefitting from a PA lifestyle intervention grounded in the Theory of Planned Behavior, this may inform future intervention studies aimed at increasing levels of moderate to vigorous PA over time.

With more than 50% of children and adolescents with surgically corrected CHD having early signs of atherosclerosis,[43] and little research identifying effective interventions to sustainably increase PA, there is a tremendous need for research on lifestyle interventions for this population. Identification of a lifestyle intervention to increase PA in CHD survivors is vital for reducing morbidity and improving quality of life. Interventions grounded in the Theory of Planned Behavior have demonstrated sustained increases in PA among other populations, including individuals with heart failure[23-25] and rural populations with multiple cardiovascular disease risk factors[26]. A few small studies[44,45] have reported positive effects of exercise training interventions on functional among adults with CHD. However, the mechanisms of these changes are unknown, limiting the ability to identify potential targets of intervention to promote sustained behavioral change. Due to the paucity of theoretically-driven interventions to improve lifestyle PA among CHD survivors, The Theory of Planned Behavior will be used as the current framework for this study. This theory will allow the identification of potential mechanisms of behavior change, such as attitudes, subjective norms and perceived control. Understanding the

circumstances in which change is more likely to occur, or the mechanisms by which it occurs, will guide both development and modification of the intervention to achieve enhanced effects in a larger clinical trial.

Thus, the long-term goal of this research study is to establish an effective intervention for sustaining increased levels of MVPA that will reduce morbidity and healthcare costs for CHD survivors. The objective of this study is to adapt a lifestyle PA intervention to transition-age young adult CHD survivors who are at greater risk for future morbidity due to having more complex disease. This will involve (1) evaluating the feasibility of the intervention and (2) obtaining qualitative feedback from participants on the content of the intervention sessions and study procedures using focus groups. We hypothesize that young adults will rate participating in as enjoyable, easy, relevant, and useful. Additionally, qualitative data about participants' study experiences will inform modifications to the session content and study procedures for the larger trial. The *rationale* for the proposed research is to obtain pilot data that will shape the next phase of investigation: determining the efficacy of this intervention for sustaining increased PA among young adult CHD survivors. Ultimately, we hope that knowledge gained from this line of research will extend longevity and optimize quality of life for CHD survivors as they age further into adulthood.

Eligible participants are 18 to 25 years of age with moderate to complex CHD. This is because individuals with moderate and complex cardiac lesions are the ones in greater need for intervention, as evidenced by significantly higher premature mortality rates as compared to the general population due to underlying cardiovascular issues.[5] Participants in the comparison arm receive a Fitbit and an exercise prescription, as well as complete the baseline, interim, and post-intervention and 6-month follow-up assessments. In addition to the Fitbit and exercise prescription, Participants in the intervention arm receive 8 20-30 min videoconferencing sessions (i.e. FaceTime, Google Hangouts or Skype) with a PA coach, which take place over the course of 20 weeks. Intervention arm participants will also be invited to partake in a focus group, which will be held via videoconferencing (2 focus groups with 5-8 participants in each group).

Using the Theory of Planned Behavior as a guide, intervention sessions focus on changing attitudes, perceptions of social norms, and perceptions of control towards PA. This theory was chosen given low PA in this population has been attributed to inaccurate negative attitudes about the consequences of PA on the heart or need for activity restriction by caregivers and others (e.g., sports coaches) during childhood.[27,28] Furthermore, poorer self-efficacy has been associated with lower levels of PA, among adults with CHD,[29] suggesting that targeting self-

efficacy may positively influence PA engagement. For the intervention arm, the Fitbit is used to facilitate goal-setting and self-monitoring while working with the PA coach. These have been used in interventions to increase PA levels among young adults with other chronic illnesses.[41,42]

2.3 Potential Risks and Benefits

2.3.1 Potential Risks

The current research study complies with the federal regulations definition of "minimal risk" [§45 CFR 46.102(i)] "that the probability and magnitude of harm or discomfort anticipated in the research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." Consequently, the CHD-PAL Study was reviewed by the NCH Institutional Review Board under §45 CFR 46.404 "Research not involving greater than minimal risk."

Exercise training has been established as safe for most CHD survivors and PA promotion in this population is highly recommended. Nevertheless, we have designed a protocol that implements several safeguards to reduce potential risk. Before a potential participant is approached for recruitment, his/her cardiologist is contacted to determine if the young adult is able to safely engage in MVPA. After receiving the cardiologist's approval and the CHD survivor is recruited, then he/she undergoes an exercise stress test to rule out the presence of arrhythmia or cardiac ischemia, which would preclude them from engaging in regular MVPA, and therefore exclude them from participating in Phase 2 of the study. Exercise stress tests are conducted within the same space used for outpatient cardiology clinic and are staffed by at least one cardiologist. As part of the exercise stress test protocol, participants are encouraged to reach the limitations of their physical capacity, which can be uncomfortable. Thus, participants are told that they may experience normal levels of physical discomfort when undergoing the exercise stress test. Upon completion of the test, participants are provided with a towel and water, and are monitored by clinical staff throughout the duration and recovery of the test. If the exercise stress test results demonstrate arrhythmia or cardiac ischemia both the participant and the participants' primary cardiologist are notified. Although learning this information could be distressing to participants, identification of an abnormality would have potential benefits to participants as well.

Similar to the exercise stress test, participants in the intervention arm may experience uncomfortable physical sensations due to exercising, including sore muscles, fatigue, and shortness of breath. If the participant has new cardiac-related symptoms since his/her last cardiology check-up that are concerning to the participant, the interventionist (i.e. PA coaches)

will recommend contacting the participant's cardiologist and the study procedures are put on hold until the cardiologist clears the participant to return to the study. The interventionist also contacts the study PI, Dr. Jackson, who notifies the participant's cardiologist that the participant is experiencing symptoms.

During videoconferencing, PA coaches conduct sessions in privacy and encourage participants to do the same. The same will be encouraged for those who participate in the focus groups. Coaches undergo the same training as other research staff at NCH, including completing Collaborative Institutional Training Initiative (CITI) certification and a day-long instructional seminar on protecting human subjects. Videoconferencing has a lower risk of privacy breach than email communications. Should technical difficulties (e.g., WiFi issues, recorder error) occur during the videoconferencing sessions, PA coaches will make adjustments in accordance with privacy and confidentiality guidelines to conduct the session and/or document the content of the session. These adjustments may include (but are not limited to) conducting the session as a voice call (in the event of videoconferencing issues) or writing a summary of the session (in the event of recorder error). Audio recordings and other documents resulting from these adjustments will be stored on the hospital's secure OneDrive platform. For the purposes of identifying and problem-solving common technical difficulties, PA coaches will record all videoconferencing, recording, and other technical and practical issues. This record will also help identify sessions that may not be available for fidelity evaluation.

Participants are informed that participation is voluntary and that they have the right to withdraw from the study at any time, as well as may refuse to answer or may skip any question(s) that cause discomfort. While not anticipated, participants could experience some discomfort when completing survey items about their heart condition or treatment history. However, this risk is very small. If discomfort occurs, it would likely be transient and minimal. Participants are encouraged to discuss any concerns about the content of the survey items with study personnel, who have experience using these questionnaires and are trained to respond appropriately. The more likely risk to participants is boredom while completing the questionnaires.

Loss of confidentiality is also a potential risk; though, no more so than in any other research study. Risks of breaching confidentiality are minimized in multiple ways. Participants are assigned a study ID number, which is used on all questionnaires (paper and online), as well as the accelerometer and Fitbit data. The only link between the participant's name and ID is an electronic tracking sheet, which is located on a password protected server on the hospital's secured research network, as well as on the hospital's secure Windows OneDrive platform.

Online questionnaire data and audio recordings of the intervention sessions are housed behind a secure firewall on the NCH research internet server and the hospitals secure OneDrive platform. All other data are kept in a locked cabinet within a locked office at the hospital and only direct study personnel have access to this information. All study personnel who are working with data or protected health information are properly trained, which includes completing the online CITI certification and undergoing a day-long instructional seminar at the hospital for protecting human subjects and engaging in best practices for responsible conduct of research.

2.3.2 Known Potential Benefits

Participants may receive direct benefit from being provided with the results of an exercise stress test and exercise prescription. Results are shared with each participant's cardiologist and entered under "research" in their medical record. Participants could also gain benefit from increasing their levels of PA. Finally, the information learned from the study could benefit future CHD survivors by possibly identifying a feasible, accessible, and acceptable intervention that can improve PA engagement in a population at risk for significant future cardiovascular morbidities.

3 OBJECTIVES

3.1 Study Objectives

A total of up to 90 young adults (ages 18 -25) are anticipated to be enrolled in Phase 1 of the study, which establishes eligibility for Phase 2. For Phase 2, the randomized trial portion of the study, we plan to enroll a total of 40 young adults. The aims of the study are to:

1. *Aim 1:* Evaluate the feasibility of the intervention.
   Hypothesis 1: Young adults will rate participating in the intervention as enjoyable, easy, relevant, and useful.

2. *Aim 2:* Obtain qualitative feedback on session content and study procedures from participants using focus groups.

3.2 Study Outcome Measures

3.2.1 Primary Outcome Measure

Enjoyment of the intervention, ease of participation, applicableness of session content, and helpfulness of the intervention.

3.2.2 Intervention Outcome Measures

Number of minutes spent in MVPA as measured by an accelerometer (primary intervention outcome).

Number of minutes spent being sedentary as measured by an accelerometer (secondary intervention outcome).

Maximal oxygen utilization during PA as measured by VO_{2max} during an exercise stress test (secondary intervention outcome).

3.2.3 Other Outcome Measures

Health-related quality of life as measured by the Patient-Reported Outcomes Measurement Information System (PROMIS).[46-48]

Self-reported PA as measured by the International Physical Activity Questionnaire (IPAQ).[49,50]

3.2.4 Purported Mechanisms

PA attitudes as measured by the Benefits of PA questionnaire[51].

PA subjective norms as measured by the PA Subjective Norms[52] and the Social Support for PA[53] surveys.

PA perceived control as measured by the Barriers to Exercise survey[54] and the Self-Efficacy for Exercise Scale.[55]

3.2.5 Other Exploratory Predictors

Cardiac-related anxiety as measured by the Cardiac Anxiety Questionnaire.[56]

Self-consciousness of body due to cardiac interventions scars as measured by the modified Body Image Disturbance Questionnaire.[57]

4 STUDY DESIGN

This single-site study is a randomized clinical trial of a Fitbit and exercise prescription vs. a Fitbit, exercise prescription, AND videoconferencing sessions with a PA coach over the course of 8 sessions in 20 weeks.

For Phase 1, participants are asked to complete less than 30-45 minutes of questionnaires wear an accelerometer for 7 days, and undergo an exercise stress test. Once the exercise stress test is completed and the accelerometer is returned, participants are compensated $100. Parking and mileage reimbursement to/from the hospital is provided.

If a participant engages in <150 minutes of MVPA per week and has no contraindications on the exercise stress test, he/she is approached for participation in Phase 2. Once recruited, participants receive a Fitbit and an explanation of their exercise prescription based on the results of their exercise stress test as provided by an exercise physiologist. If the exercise physiologist is not available to develop the exercise prescription, the principal investigator, in consultation with the study physician, will develop the exercise prescription based on guidelines provided by the exercise physiologist. Next, study staff open an envelope (pre-prepared by the study statistician, Dr. Rausch) to reveal the participant's study arm designation. Randomization is stratified by the number of minutes spent in MVPA per the accelerometer data in Phase 1 ($\leq$25 min/day of MVPA vs. $\geq$26-59 min/day of MVPA) with randomly varying block sizes.

Participants are randomized to 1 of 2 arms: the comparison arm, which receives a Fitbit and the exercise prescription, or the intervention arm, which also receives a Fitbit and exercise prescription PLUS videoconferencing sessions (e.g., FaceTime, Google Hangouts or Skype) with a PA coach (8 sessions over the course of 20 weeks). Each session lasts approximately 30 minutes and is audiotaped. The intervention arm focuses on changing attitudes (e.g., identifying pleasurable physical activities), perceptions of social norms of PA (e.g., problem-solving ways to receive support from family and friends) and perceptions of control for engaging in PA (e.g., increasing self-efficacy through goal setting and reducing barriers), as outlined by the Theory of Planned Behavior, to increase time spent in MVPA and decrease SB. The Fitbit is used to facilitate goal setting and self-monitoring for participants in the intervention arm.

During the course of the study, participants in both arms are asked to participate in an interim assessment (between weeks 8-12), which includes 30-45 minutes of questionnaires and wearing an accelerometer for 7 days, for which they are compensated $50. Between weeks 20 and 26, participants in both arms are asked to engage in a post-intervention assessment, consisting of 30-

45 minutes of questionnaires, wearing an accelerometer for 7 days, and undergoing a final exercise stress test. Participants are compensated $100. Parking and mileage to/from the hospital is compensated for their final exercise stress test. Upon completion of the post-intervention assessment, participants randomized to the intervention arm will be asked to participate in focus groups lasting approximately 1.5 hours, to discuss their study experiences. There will be 2 groups that meet via videoconferencing with 5-8 participants per group. Participants who attend the focus group will be compensated $50.

Medical information also is collected from participants' online medical records to consider as covariates or moderators of the treatment effect, including sex and indicators of disease status (e.g., diagnosis, surgical history, functional class, number of medications, comorbidities, and the number of hospitalizations in the past year).

Physical activity coaches are graduate students pursuing advanced degrees in medicine, exercise physiology, or other health-related fields. They have undergone over 16 hours of training prior to working with the first participant and have completed all required human subjects training.

5 STUDY ENROLLMENT AND WITHDRAWAL

The total target sample size for enrollment in Phase 1 is up to 90 participants and in Phase 2, 40 participants (~17 participants per arm). A higher enrollment is expected for Phase 1 than Phase 2 to account for some participants being deemed ineligible to proceed with Phase 2.

Potential participants are identified through upcoming cardiology clinic rosters who meet the age (18 – 25 years of age) and diagnosis (moderate to complex CHD[3]) criteria. Study personnel check the patient's medical record to verify eligibility. If a patient appears to be eligible, study staff confirm with the attending cardiologist that no additional reason/s preclude the young adult from participating, including limitations to engaging in MVPA. Next, the patient is sent a letter from the attending cardiologist, notifying them about the study and that study personnel will be in contact. An "opt out" phone number is provided so that the potential participant can call and leave a message if they do not wish to be contacted. Approximately 1 week later, if no message was received, patients are called by study personnel. During the phone conversation, the objectives and primary components of the study are discussed. If a patient is interested, verbal consent is obtained for completing online questionnaires and the exercise stress test at NCH is scheduled. During the stress test visit, written consent for the stress test and accelerometer assessment is obtained. If a patient cannot be reached via phone, they are approached during their clinic appointment in person.

5.1 Participant Inclusion Criteria

Participants must meet all the inclusion criteria to be eligible to participate in the study. The criteria include:

1) Between 18 and 25 years of age
2) Diagnosed with moderate or complex structural CHD
3) Lives within 120 miles of NCH
4) Able to complete an exercise stress test on a treadmill

5.2 Participant Exclusion Criteria

Participants meeting any of the exclusion criteria at baseline will be excluded from the study. These criteria include:

1) Do not speak and write proficiently in English
2) Have a diagnosis of a genetic syndrome (e.g., Downs, Marfans, Wolf-Parkinson-White)
3) Have cognitive impairments that would interfere with completion of study measures
4) Have been engaged in a formal exercise program within the past 6 months, including cardiac rehabilitation
5) Have undergone open-heart surgery or have had a valve replacement in the last 3 months
6) Are prohibited to engage in MVPA by their cardiologist
7) Are unable to complete a treadmill-based exercise stress test
8) Are currently pregnant

After completing Phase 1, participants are approached for recruitment into Phase 2 unless they meet additional exclusion criteria, including:

9) Having contraindications for exercise based on an exercise stress test (e.g., exercise-induced arrhythmias or evidence of cardiac ischemia)
10) Exercising >150 min/week of MVPA per the accelerometer
11) Do not have internet access or a device for videoconferencing with a PA coach

5.3 Treatment Assignment Procedures

5.3.1 Randomization Procedures

The PI, study staff, and the research participant do not know the participant's arm designation until the envelope, which was prepared the by the study statistician (Dr. Rausch) is opened.

Randomization is stratified by the number of minutes spent in MVPA per the accelerometer data in Phase 1 (≤25 min/day of MVPA vs. ≥26-59 min/day of MVPA) with randomly varying block sizes. Strata were based on the mean baseline levels of MVPA as reported in 2 studies of young and middle-aged adults with CHD.[19,29]

5.3.2 Reasons for Withdrawal

Study participation is discontinued under the following circumstances:

- If participant's cardiologist determines that he/she is no longer eligible for the study due to a change in his/her cardiac condition.
- The participant requests withdrawal from the study.
- Development or reveal of any exclusion criteria (e.g., need for cardiac surgery).

5.3.3 Handling of Withdrawals

If withdraw occurs because a participant's cardiologist determines that the participant should no longer be in the study due to a change in medical status or the participant requests to be withdrawn, participants are asked to complete the assessments if possible and are included in intent-to-treat analyses.

5.3.4 Termination of Study

Because the AHA and American College of Cardiology indicate that receiving an exercise stress test is a standard of care and that CHD survivors with moderate to complex disease should be engaged in routine PA as long as it is deemed safe,[7] termination of the study due to the development of adverse events is not anticipated. There are several procedures aimed to rule out any participants who may be at an increased risk of an adverse event due to the intervention. First, participants' cardiologists are asked about the eligibility of each potential participant. Second, participants undergo a baseline exercise stress test, in part, to rule out any cardiovascular contraindications for PA. If limitations in PA exist, these are incorporated into the exercise prescription developed by the exercise physiologist who conducted the stress test/principal investigator in consultation with the study physician, and the PA coaches work with participants on PA within the parameters of the exercise prescription. Participants' cardiologists have access to the results of the stress test, which are posted in participants' electronic medical record. However, the study will be terminated if the Data Safety Monitoring Board (DSMB) or IRB concludes, based on their findings, that termination is in the best interest of the participants.

5.4 Study Intervention Description

During the Phase 2 of the study participants are randomized into the comparison or intervention arm. Both the comparison and intervention arm participants receive a Fitbit and are asked to complete the interim (between weeks 8-12) and post-intervention (between weeks 20-26) assessments. In addition, the intervention group is asked to complete 8 videoconferencing sessions with a PA coach over 20 weeks (Sessions 1-4 occur weekly; Session 5 is in week 6; Session 6 is in week 8; Session 7 is in week 12; Session 8 is in week 20) with each session lasting approximately 20-30 minutes. Intervention participants who complete the protocol will also be invited to partake in a focus group after the post-intervention assessment has been completed to provide feedback on their study experiences. The topics for the intervention sessions focus on helping participants to:

1) Understand the benefits of MVPA, find physical activities they enjoy, and delineate pros and cons of engaging in MVPA using a non-judgmental stance (*Attitudes*)
2) Trouble-shoot engaging family and friends to be supportive of or engage in PA with the participant (*Subjective Norms*)
3) Find creative ways to incorporate more MVPA, resolve barriers to PA and promote efficacy for engaging in MVPA, and identify intrinsic rewards for accomplishing goals (*Perceived Control*)

All of the sessions contain a goal-setting component based on the exercise prescription the participant obtained from his/her exercise stress test. Participants receive text messages in between sessions, which contain motivational or encouraging content.

5.4.1 Session Description

Session 1 (Week 1)

Coaches inquire about participants' attitudes about PA and encourage them to get familiarized with their Fitbit.

Session 2 (Week 2)

Participants' are encouraged to discuss their knowledge about PA and to think about pros and cons for engaging in PA. Goals are set in collaboration with the participant, including increasing participants' PA frequency, duration, or intensity.

Session 3 (Week 3)

Coaches inquire about participants PA self-efficacy/perceived control by asking what gets in the way of engaging in activities that the participant enjoys and troubleshoot around controllable

barriers. Participants are also encouraged to try a new type of PA. Goals are set for increasing frequency, duration, or intensity when engaging in PA.

Session 4 (Week 4)

Coaches will inquire about participants PA subjective norms (e.g., “Have you talked with your caregivers/siblings/friends/cardiologist about being active?” “What do they think about you being active?”), and are encouraged to talk to family/friends/cardiologist about being active if they have not, as well as invite family/friends to join them in physical activities. Goals are set to increase frequency, duration, or intensity of PA.

Session 5 (Week 6)

Coaches promote participants’ independence by modeling the use of core concepts from the Theory of Planned Behavior learned in Sessions 1-4 with emphasis placed on managing barriers and promoting boosters to PA. Participants are encouraged to increase frequency, duration, or intensity of PA based on what they perceived as being the easiest to increase.

Session 6 (Week 8)

Coaches continue promoting participants’ independence by discussing the process of goal-setting, including making achievable goals and anticipating barriers. Participants are asked to set up his/her goals in respect to increase frequency, duration, or intensity of PA.

Session 7 (Week 12)

Coaches continue promoting participants’ independence by reflecting about their progress and discussing the process of setting long-term goals. Participants are encouraged to set new goals ever 2 weeks during the span between Session 7 and 8. Coaches help participants identify potential barriers to achieving their goals, as well as how they can continue to use their Fitbit for self-monitoring.

Session 8 (Week 20)

Coaches summarize the intervention, focusing on the participant’s successes and gains. Coaches will also inquire about participants’ motivation and promote maintenance.

5.5 Modification of Study Intervention

Modifications to the study intervention may occur if a participant experiences a change in their cardiac health during the course of the study and his/her cardiologist recommends an alteration in the participant’s exercise prescription.

5.6 Accountability Procedures for the Study Intervention

Individual and group supervision sessions are held for coaches to clarify study procedures, receive feedback on interactions with participants, and share ideas for ways to trouble-shoot around barriers to PA that participants broach during session. Dr. Vannatta, who is familiar with the study but is not directly involved, as well as another study staff member, will listen to a random selection of 2 audiotaped sessions per participant and rated on their fidelity. Fidelity <90% triggers retraining of the interventionist as to the study materials.

5.7 Assessment of Subject Compliance with Study Intervention

Participant compliance in the intervention arm is monitored in two ways. First, participants are asked to wear a Fitbit, which is used by the coaches to assess the participants' engagement in MVPA. Coaches request that participants in the intervention arm sync their Fitbit each day so that coaches may monitor their PA levels and incorporate feedback during sessions. Participants' attendance at each session is documented. For those participants in the comparison arm, they are told to sync their Fitbit regularly upon first receiving the Fitbit, but are not contacted about the Fitbit again.

5.8 Concomitant Treatments

Given the primary and secondary outcomes of the study, participants who are currently or have engaged in a formal exercise program in the past 6 months, including cardiac rehabilitation, are not able to participate in the study. Engaging in sports during the study is not an exclusionary criterion.

6 STUDY SCHEDULE, STUDY PROCEDURES/ EVALUATIONS

6.1 Screening

Potential participants are identified through scheduled clinic appointments for the upcoming month. Study personnel first identify patients who meet the age criteria and then check the patient's medical record to verify their eligibility based on the inclusion and exclusion criteria. If a patient appears to be eligible the cardiologist confirms that they do not know of any reason the patient should not participate in this research, including limitations to engaging in MVPA. The patient is then sent a letter from the attending cardiologist, notifying them about the study and that study personnel will be in contact.

6.2 Phase 1: Enrollment/Baseline (T1)

Once the participant has consented, they are asked to complete an online questionnaire. The participant is also asked to undergo an exercise stress test and wear an accelerometer for 7 days. The stress test is completed at NCH within 3-4 weeks of recruitment and standardized feedback will be provided by an exercise physiologist, which includes their VO_{2max}. Once completed, participants are compensated $100 for their time for the baseline assessment.

Baseline online questionnaire:

- Socio-demographics characteristics
- Benefits of PA[51]
- Subjective Norms survey[52]
- Social Support for Exercise survey[53,55]
- Barriers to Exercise survey[54]
- Self-Efficacy for Exercise Scale[55]
- Patient-Reported Outcomes Measurement Information System[46-48]
- International Physical Activity Questionnaire[49,50]
- Cardiac Anxiety Questionnaire[56]
- Modified Body Image Disturbance Questionnaire[57]
- Physical Activity Stages of Change Questionnaire – Algorithm[58]
- Physical Activity Stages of Change Questionnaire - Continuous[59-61]

VO_{2max}: VO_2 measurement is obtained via a graded exercise stress test on a treadmill. Exercise stress test results are used by the exercise physiologist to devise an exercise prescription that consists of recommendations for frequency, duration, intensity and type of PA. Exercise prescriptions are provided to participants if they qualify and enroll in Phase 2. Participants who are found to have an arrhythmia or show evidence of cardiac ischemia during exercise stress testing are immediately referred to their cardiologist for follow-up and are not be eligible for Phase 2.

MVPA and SB: Participants receive a triaxial accelerometer (ActiGraph, model wGT3X-BT), sensitive to movement in all directional planes, to measure the amount of time spent in sedentary, light, moderate, and vigorous PA. The accelerometer is worn around the waist for 7 days for at least 10 hours per day, only to be removed when showering or submerging in water (e.g., swimming). Participants will also complete self-monitoring PA logs in the case they cannot wear the accelerometer (e.g. swimming). If baseline accelerometer and self-monitor PA log data indicate that a participant averages at least 150 minutes of MVPA per week, they are not eligible for Phase 2.

Compensation: Participants are compensated $100 for completing the baseline survey, exercise stress test, and wearing the accelerometer for at least 4 days (1 weekend day, 3 weekdays), for at least 10 hours per day. Additionally, participants' parking and mileage to/from the hospital for the exercise stress test are reimbursed.

Contact and Scheduling. If the participant is eligible for the Phase 2, they are contacted by phone and asked to schedule a home visit, within 8 weeks from their exercise stress test, if interested in participating.

6.3 Phase 2: Enrollment in the RCT

Eligible participants from Phase 1 are met at their home (or the hospital if preferred) to receive their Fitbit and exercise prescription, which is based on the results of their stress test. Home visits may also be conducted virtually (e.g., via Google Hangouts). Participants completing virtual home visits will receive study materials by postal mail or email as appropriate. After receiving the Fitbit and exercise prescription, the participant's arm designation is revealed by opening an envelope that has been prepared by the study statistician, Dr. Rausch. Prior to opening the envelope, the study PI, study staff, and the participant are blind to the study arm designation.

6.4 Interim Assessment (between weeks 8-12)

Participants in both arms are asked to complete an interim assessment (between weeks 8-12), which includes:

Interim online questionnaire: Participants are asked to complete the same questionnaire that was completed at Baseline, with the exception of those in the comparison arm receiving questions about changes to their health since Baseline.

Benefits of PA[51]
Subjective Norms survey[52]
Social Support for Exercise survey[53]
Barriers to Exercise survey[54]
Self-Efficacy for Exercise Scale[55]
Patient-Reported Outcomes Measurement Information System[46-48]
International Physical Activity Questionnaire[49,50]
Cardiac Anxiety Questionnaire[56]
Changes in Health
Physical Activity Stages of Change Questionnaire – Algorithm[58]
Physical Activity Stages of Change Questionnaire - Continuous[59-61]

MVPA and SB: Participants wear an accelerometer again for the same period (7 days) as the Baseline assessment and complete self-monitoring PA logs in the case they cannot wear the accelerometer (e.g. swimming).

Compensation: Participants are compensated $50 for completion of the interim assessment survey and wearing the accelerometer for at least 4 days (1 weekend day, 3 weekdays), for at least 10 hours per day.

6.5 **Post-Intervention** (between weeks 20-26)

Participants in both arms are asked to complete a post-intervention assessment (between weeks 20-26), which includes:

Post-intervention online questionnaire: Similar items are included on the post-intervention questionnaire as with the baseline and interim assessment with the exception that participants are asked to rate the intervention on multiple dimensions.

Benefits of PA[51]
Subjective Norms survey[52] Social Support for Exercise survey[53]
Barriers to Exercise survey[54]

Self-Efficacy for Exercise Scale[55]
Patient-Reported Outcomes Measurement Information System[46-48]
International Physical Activity Questionnaire[49,50]
Cardiac Anxiety Questionnaire[56]
Changes in Health
Post-Intervention Satisfaction
Physical Activity Stages of Change Questionnaire – Algorithm[58]
Physical Activity Stages of Change Questionnaire - Continuous[59-61]

MVPA and SB: Participants wear an accelerometer again for the same measurement period (7 days) as in previous assessments and complete self-monitoring PA logs in the case they cannot wear the accelerometer (e.g. swimming).

VO_{2max}: VO_2 measurement is obtained again with a graded exercise stress test using a modified Bruce protocol. Participants who were found to have an arrhythmia or show evidence of cardiac ischemia during exercise stress testing will be immediately referred to their cardiologist for follow-up.

Compensation: Participants are compensated $100 for completion of the post-intervention survey, exercise stress test, and returning the accelerometer with at least 4 days (1 weekend day, 3 weekdays), for at least 10 hours per day of data. Additionally, participants parking and mileage to/from the hospital for the exercise stress test are reimbursed.

6.6 **Focus Groups** (after post-intervention assessment)

Participants in the intervention arm are asked to partake in a focus group lasting approximately 1.5 hours, to discuss their experiences in the study. There will be 2 groups that meet via videoconferencing with 5-8 participants per group.

Compensation: Participants are compensated $50 for being in the focus group.

6.7 Additional Incentive

In addition to the compensation described in sections 6.2, 6.4, and 6.5, participants in both arms are able to keep the Fitbit.

7 ASSESSMENT OF SAFETY

7.1 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters

7.1.1 Adverse Events

Definition

For the current study, an adverse event is an unanticipated change in cardiovascular, musculoskeletal, or emotional symptoms that are (1) concerning to the participant and (2) results in seeking medical attention, if cardiovascular or musculoskeletal in nature. Any condition that is present at the time that the participant is screened will be considered as baseline and not reported as an adverse event. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an adverse event. Serious adverse events are defined as adverse events that are severe in classification (as described below). We do not anticipate any serious adverse events due to study procedures. Adverse events that occur for participants during the course of the study are comprehensively documented, including events during the stress test, symptoms reported during the course of the intervention from participants in the intervention arm, dates and reasons for pauses in the study protocol due to symptom reporting, and determination of ability to proceed by participants' cardiologists. All unscheduled cardiology outpatient visits, visits to urgent care or the emergency department, unscheduled hospitalizations, or any other changes in health are documented. Participants in the comparison arm are asked whether they sought medical attention in the aforementioned contexts during the interim and post-intervention questionnaires. Additionally, the occurrence of any adverse event or serious adverse event may come to the attention of study staff during other study contacts (e.g., intervention meetings).

Classification

All adverse events and serious adverse events will be assessed by the PI and the study physician, Dr. Clifford Cua, according to the guidelines outlined here.

Severity: The following guidelines will be used to describe severity:

- Mild: Events require minimal or no treatment and do not interfere with the participant's daily activities.
- Moderate: Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- Severe: Events that require in-patient hospitalization and/or resulted in death or permanent disability.

Relationship to Study Intervention: The degree of certainty about causality will be graded using the categories below.

- Related: The adverse event is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the adverse event, or there is a temporal relationship between the study procedures and the adverse event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the adverse event.
- Not Related: There is not a reasonable possibility that the study procedures caused the adverse event, there is no temporal relationship between the study procedures and adverse event onset, or an alternate etiology has been established.

Expectedness: It is determined whether an adverse event is expected or unexpected, according to the following criteria.

- Expected: Adverse event is consistent with the risk information previously described for the study procedures.
- Unexpected: Adverse event is not consistent with the risk information previously described for the study procedures.

Safety Procedures

The current study has several procedures in place to reduce the likelihood of serious medical adverse events. Potential participants' cardiologists are notified prior to being recruited for the study and excluded if the cardiologist has communicated or documented any concerns about that young adult engaging in MVPA. All participants undergo a baseline exercise stress test and are not approached for recruitment for Phase 2 if contraindications are detected in Phase 1. In the rare event that a participant has an acute medical event during the exercise stress test, appropriate hospital procedures are enacted, which include calling an emergency response team and immediate evaluation by a cardiologist. The same procedures used for patients undergoing exercise stress testing as part of a medical evaluation are initiated and followed. During the course of the intervention, if a young adult reports cardiac symptoms that are concerning to the participant and are new since the last cardiac evaluation, PA coaches are trained to request that the young adult contact their cardiologist. Young adults have given the study PI, Dr. Jackson, permission to talk with the cardiologist in the instance that a concerning and/or new cardiac symptom is reported. All study procedures are put on hold until the young adult is evaluated by the cardiologist and cleared to proceed with the study.

If a participant was to report bothersome emotional symptoms to study staff during the course of the study, Dr. Jackson, a licensed psychologist, will contact the participant to evaluate the severity of their emotional symptoms. If the participant is not in danger of harming themselves or someone else, Dr. Jackson will assist the participant in identifying mental health resources. If the participant is positive for significant suicidal or homicidal ideation (i.e., positive for intent, has a plan, and has the means by which to execute a plan), Dr. Jackson will notify the participant that confidentiality must be broken and the local authorities will be contacted.

7.1.2 Procedures to be Followed in the Event of Abnormal Test Values or Abnormal Clinical Findings

Incidental findings from the exercise stress test are communicated to the participant and the participant's cardiologist. The cardiologist will make a determination as to whether the participant may proceed with the study if an abnormal event, or incidental finding, is detected.

7.1.3 Other Medical Events

Medical events not meeting the above definition of an adverse event.

7.1.4 Unanticipated Problems

In line with the OHRP definition, unanticipated problems include any incident, experience, or outcome that meets **all** of the following criteria:

1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

2. related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

7.2 Reporting Procedures

7.2.1 Adverse Events

Any adverse events are reported to the DSMB at each meeting and to the NCH IRB annually.

7.2.2 Serious Adverse Events

The DSMB is notified of any serious adverse events determined to be related to the intervention and are unexpected within 5 business days of discovery. Other serious adverse events are reported to the DSMB at each meeting.

Similarly, and per the NCH HRP-103 (updated 12/10/2018), serious adverse events determined to be related to the intervention and are unexpected are reported to the NCH IRB within 5 business days of discovery. Other serious adverse events are reported to the NCH IRB annually.

Serious adverse events that are fatal or life-threatening and are unexpected are reported to NHLBI within 7 calendar days of discovery by the investigator. For non-fatal, non-life-threatening unexpected, serious adverse events, NHLBI is notified within 15 calendar days, by the investigator.

7.2.3 Unanticipated Problems

Any unanticipated problems that are not serious adverse events will be reported to the DSMB within 2 weeks and to NHLBI within 14 days by the investigator. If an unanticipated event *is* considered a serious adverse event, the aforementioned reporting time for serious adverse events will be followed.

7.3 Type and Duration of Follow-up of Subjects after Adverse Events and Unanticipated Problems

Participants will be monitored for adverse events and unanticipated problems from the start of the intervention in Phase 2 until the post-intervention assessment that occurs 22 weeks after the start of the intervention, as this signifies study completion. Adverse events and unanticipated problems will be followed until stabilization or resolution, or 30 days after study completion (whichever occurs sooner).

All cardiac-related adverse events and unanticipated problems are discussed with the cardiology medical team. The cardiology medical team determines whether participation in the study is suspended, and for how long, or terminated.

7.4 Halting Rules

If it is found that the study intervention is related to an unexpected serious adverse event, an ad hoc meeting will commence that will include the PI, study physician, and the DSMB to determine if enrollment needs to be temporarily suspended until a safety review is convened. If a safety review is conducted, the DSMB will decide whether the study should continue per protocol, proceed with

caution, be further investigated, be discontinued, or be modified and then proceed. Suspension of enrollment (for a particular group or for the entire study) is another potential outcome of a safety review.

7.5 Safety Oversight

Safety oversight of this study is under the direction of the study PI, NCH IRB, as well as a DSMB. The DSMB consists of two faculty members from NCH and a faculty member from the University of Notre Dame. Dr. May Ling Mah is a dual-boarded pediatric and adult congenital cardiologist housed in the Heart Center at NCH. Dr. Mark Klebanoff is a board-certified pediatrician and a former Director of the Division of Epidemiology, Statistics, and Prevention Research at the National Institute of Child Health and Human Development. Dr. Klebanoff has been involved as a Co-I of multiple RCTs and currently serves on the DSMB for an NIH-funded clinical trial. Dr. Ken Kelley is a Professor in the Department of Psychology, an Associate Dean for Faculty and Research in the Mendoza College of Business at the University of Notre Dame, and is an accredited professional statistician per the American Statistical Association. Dr. Kelley currently serves on several DSMBs for NIH-funded clinical trials. The NCH IRB has reviewed and approved the Data and Safety Monitoring Plan for this study. Bi-yearly reports summarizing the number of participants enrolled, the number of stress tests completed, the number of abnormalities detected during exercise stress testing, adverse events and serious adverse events, and the number of participants who have contacted their cardiologists due to concern over symptoms while engaged in the treatment arm will be provided to the DSMB. This summary is submitted to the IRB with the annual review.

7.6 Study Hypotheses

Hypothesis 1: Young adults are hypothesized to rate the intervention as enjoyable, easy, relevant, and useful.

7.7 Sample Size Considerations

The sample size of 40 for the Phase 2 RCT component is obtainable in the 2-year timeframe of this study and is adequate for addressing the study aims for determining feasibility (i.e., intervention acceptability, recruitment rate, retention rate, intervention session adherence, and assessment completion rate). The current sample size is not powered to detect treatment effects and is not

intended to be used for effect size estimation due to the risk of under or overestimating the sample size for the larger study[62,63].

Planned Interim Analyses (if applicable)

No interim analysis is planned.

7.8 Analysis Plan

Aim 1: Evaluate the feasibility of the intervention.

Objective indicators of feasibility will be evaluated, including recruitment rate (# recruited divided by # approached), adherence to intervention sessions (% sessions completed per participant), retention rate (# drop outs divided by # randomized) and assessment completion rate (% of participants who completed each assessment and the timeframe in which completed). Participants will also rate the intervention on multiple dimensions, and mean/median ratings will be computed.

Aim 2: Obtain qualitative feedback on session content and study procedures from participants using focus groups.

Focus group feedback will be transcribed and coded. Themes will be identified using 2 coders, and the number of participants who endorse a theme will be tabulated.

8 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

All study related records are kept in compliance with the regulatory and institutional requirements of confidentiality of subjects. Examples of these original documents and data records include but are not limited to: hospital records and recorded data from surveys, accelerometers, Fitbits, videoconferencing sessions, and focus groups. Also, only authorized study personnel and NCH IRB staff have access to the records, all of whom have received training on the responsible conduct of human subject research.

9 QUALITY CONTROL AND QUALITY ASSURANCE

The quality management program for this study consist of a system of quality checks on all data collection procedures, in addition to a system of training.

All study personnel working with data or protected health information have been properly trained, including completing the online CITI certification and undergoing a day-long instructional seminar at the hospital for protecting human subjects and engaging in best practices for responsible conduct of research. Furthermore, PA coaches have undergone over 16 hours of training prior to working with the first participant and have completed all required human subjects training.

At periodic intervals, the quality of the videoconferencing sessions will be evaluated by Dr. Vannatta and another research staff member. They will listen to two randomly selected sessions for each participant. These evaluations will consist of completing a fidelity checklist to evaluate compliance/adherence to the session protocol.

10 ETHICS/PROTECTION OF HUMAN SUBJECTS

10.1 Ethical Standard

The investigator will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR Part 46 and/or the ICH E6; 62 Federal Regulations 25691 (1997).

10.2 Institutional Review Board

The NCH IRB has reviewed and approved the protocol for this study, including all associated documents such as the informed consent/assent, surveys, and work sheets for the videoconferences. Study amendments will be approved by the NCH IRB prior to implementing any edits to the study protocol or associated documents.

10.3 Informed Consent Process

Potential participants are identified through a list of all patients who meet the age and diagnosis criteria. Once the list has been generated, study personnel check the patient's medical record, as well as contact the patient's cardiologist, to verify their eligibility. If a patient appears to be eligible, the patient is sent a letter from the attending cardiologist, notifying them about the study and that study personnel will be in contact. An "opt out" phone number on the letter is provided so that the patient can call and leave a message if they do not wish to be contacted. Approximately 1 week later, if no message was received, the patient is called by study personnel. During the phone conversation, the objectives and primary components of the study are discussed. Also, potential participants are reminded of their rights as a participant, including that nonparticipation will not impact their care at NCH. If the patient is interested, verbal consent is obtained for completing the online questionnaires and the exercise stress test is scheduled. During the stress test, written consent for using the accelerometer and undergoing the stress test is obtained from participants. Participants retain a copy of consent forms for their own records.

10.4 Subject Confidentiality

Subject confidentiality is strictly held by the PI, study personnel, as well as the sponsor(s) and their agents. The study protocol, data, and all other information generated is held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party.

A study monitor or other authorized representatives may inspect all documents and records maintained. Records will be retained until it has been determined that those participants would not be contacted for follow-up or other relevant studies.

10.5 Study Discontinuation

If the DSMB were to determine that the study procedures were producing more harm than good for participants, the study would be discontinued.

11 DATA HANDLING AND RECORD KEEPING

11.1 Data Management Responsibilities

The PI is responsible for ensuring the accuracy, completeness, legibility (if applicable), and timeliness of the data reported. All study data is reviewed by the study personnel, who ensure that the obtained information is accurate and complete.

Additionally, study personnel are responsible for the data management, quality review, analysis, and reporting of the study data under the direction of the PI.

11.2 Data Capture Methods

For the purposes of this study, data is captured via paper and/or electronic methods. The only link between the participants' name and ID is an electronic tracking sheet, which is stored on the password protected hospital network and hospital OneDrive. All questionnaire data is stored in REDCap, a secure web application for building and managing online surveys and databases. Fitbit data is stored in Fitabase, a comprehensive online data management platform. Accelerometer data, along with the exported questionnaire, Fitbit data, and audio recordings of the focus groups are stored in the hospital's secured research network. The audio recordings of the videoconferencing sessions are housed in the hospital's secure OneDrive. All other data is kept in a locket cabinet within a locked office at NCH and only direct study personnel have access to this information.

Also, study personnel will conduct internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate.

11.3 Types of Data

Data for this study include questionnaires (electronic or pen and paper), medical record, audio recordings, and other forms of electronic data from accelerometers, Fitbits, sessions, and the exercise stress tests.

11.4 Study Records Retention

Study records are kept on the hospital's secured research network and OneDrive until it has been determined that those participants would not be contacted for follow-up or other relevant studies.

11.5 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, Good Clinical Practice, or Manual of Procedures requirements. The noncompliance may be either on the part of the subject, the investigator, or the study personnel. As a result of deviations, corrective actions are to be implemented promptly.

All deviations from the protocol must be addressed in study source documents and are documented. Protocol deviations are sent to the IRB per their guidelines.

12 PUBLICATION POLICY

Following completion of the study, the PI anticipates publishing the results of this research in a scientific journal. The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a trials-registration policy as a condition for publication. This policy requires that all clinical trials be registered in a public trials registry such as ClinicalTrials.gov*, which is sponsored by the National Library of Medicine.

13 PROTECTED HEALTH INFORMATION RECORDING

1.0 Indicate which subject identifiers will be recorded for this research.

- ☒ Name
- ☒ Complete Address
- ☒ Telephone or Fax Number
- ☐ Social Security Number (do not check if only used for ClinCard)
- ☒ Dates (treatment dates, birth date, date of death)
- ☒ Email address , IP address or url
- ☒ Medical Record Number or other account number
- ☐ Health Plan Beneficiary Identification Number
- ☐ Full face photographic images and/or any comparable images (x-rays)
- ☐ Account Numbers
- ☐ Certificate/License Numbers
- ☐ Vehicle Identifiers and Serial Numbers (e.g. VINs, License Plate Numbers)
- ☐ Device Identifiers and Serial Numbers
- ☒ Biometric identifiers, including finger and voice prints
- ☐ Other number, characteristic or code that could be used to identify an individual
- ☐ None (Complete De-identification Certification Form)

2.0 Check the appropriate category and attach the required form* on the Local Site Documents, #3. Other Documents, page of the application. (Choose one.)

- ☒ Patient Authorization will be obtained.
- ☒ Protocol meets the criteria for waiver of authorization.
- ☐ Protocol is using de-identified information.
- ☐ Protocol involves research on decedents.
- ☐ Protocol is using a limited data set and data use agreement.

3.0 How long will identifying information on each participant be maintained?

Identifying information will be maintained on each participant until it has been determined that those participants would be contacted for follow-up or other relevant studies.

For potential participants who declined participation, identifying information will be maintained until the main study results have been published after peer review.

4.0 Describe any plans to code identifiable information collected about each participant.

Participants will be assigned a study ID number, which will be used on all questionnaire (paper or online) and accelerometer data (including data from the Fitbit). The only link between the participant's name and ID will be an electronic tracking sheet, which will be

stored on the password protected hospital network and hospital OneDrive. Online questionnaire data and digital recordings of videoconferencing sessions will be housed behind a secure firewall on the password protected NCH research internet server. All other data will be kept in a locked cabinet within a locked office at NCH and only direct study personnel will have access to this information. All study personnel who will be working with data or protected health information will be properly trained, which includes completing the online Collaborative Institutional Training Initiative certification and undergoing a day-long instructional seminar at the hospital for protecting human subjects and engaging in best practices for responsible conduct of research.

During videoconferencing, coaches will conduct sessions in privacy and will encourage participants to do the same. Coaches will undergo the same training as other research staff at NCH, including completing CITI certification and a day-long instructional seminar on protecting human subjects. Videoconferencing has a lower risk of privacy breach than email communications.

5.0 Check each box that describes steps that will be taken to safeguard the confidentiality of information collected for this research:

☒ Research records will be stored in a locked cabinet in a secure location

☒ Research records will be stored in a password-protected computer file

☒ The list linking the assigned code number to the individual subject will be maintained separately from the other research data

☒ Only certified research personnel will be given access to identifiable subject information

6.0 Describe the provisions included in the protocol to protect the privacy interests of subjects, where "privacy interests" refer to the interest of individuals in being left alone, limiting access to them, and limiting access to their information. (This is not the same provision to maintain the confidentiality of data.)

When potential participants are first notified about the study via a letter from their cardiologist or the research team, there will be an opt out number provided. This will allow participants to notify the study team if they are not interested in being approached.

During the consent process, participants will be told about what information will be collected and that they can withdraw permission for study staff to access that information at any time.

For those who decline participation, they will no longer be contacted by study staff. Information will be gleaned from their medical charts around the time of decline and would not be accessed again unless clarification of the data collected is needed.

Confidential Health Information

1.0 Please mark all categories that reflect the nature of health information to be accessed and used as part of this research.

☒ Demographics (age, gender, educational level)

☒ Diagnosis
☒ Laboratory reports
☐ Radiology reports
☐ Discharge summaries
☒ Procedures/Treatments received
☒ Dates related to course of treatment (admission, surgery, discharge)
☐ Billing information
☒ Names of drugs and/or devices used as part of treatment
☒ Location of treatment
☒ Name of treatment provider
☒ Surgical reports
☐ Other information related to course of treatment
☐ None

2.0 Please discuss why it is necessary to access and review the health information noted in your response above.

Confidential health information will be accessed and reviewed in order to determine eligibility, determine disease severity, and described the clinical characteristics of the sample. Disease severity and other medical information may be used as a covariate in the analyses.

Confidential heath information will also be accessed and reviewed to determine whether those who decline participation vary significantly in disease severity, athletic involvement, or distance form NCH. Ultimately, this information will be used to alter future iterations of the intervention.

3.0 Is the health information to be accessed and reviewed the minimal necessary to achieve the goals of this research? ☒ Yes ☐ No

4.0 Will it be necessary to record information of a sensitive nature? ☐ Yes ☒ No

5.0 Do you plan to obtain a federally-issued Certificate of Confidentiality as a means of protecting the confidentiality of the information collected? ☒ Yes ☐ No

This study is funded by the National Institutes of Health and is therefore automatically issued a Certificate of Confidentiality.

14 TEMPORARY CHANGES IN PROTCOL IN RESPONSE TO THE COVID-19 PANDEMIC

Pursuant to the communications “Research Continuity During the COVID-19 Pandemic #1” (3/13/2020) and “Research Continuity During the COVID-19 Pandemic #2 (3/16/2020), and in order to eliminate potential hazard to research participants, the CHD-PALS will enact the following procedures, effective **3/13/2020**:

- Scheduled in-person home visits will be canceled and will instead be conducted remotely via videoconferencing (e.g., Google Hangouts). The IRB has previously approved the use of videoconferencing for the delivery of lifestyle interventions in this study. Videoconferencing has been reviewed by the NCH security team and was determined to have a lower risk of privacy breach than email communications. In-person home visits will resume when determined safe by NCH.
- Study materials necessary to complete the virtual home visit (e.g., consent forms, FitBit, lifestyle intervention sessions notes) will be sent to participants via postal mail or e-mail in advance of the visit. Study staff will confirm participant’s mailing address prior to sending materials via postal mail. Materials sent via postal mail will be issued tracking numbers, and study staff will monitor the status of these materials.
- Participants will provide written informed consent during the virtual home visit. As noted above, consent forms will be mailed to participants prior to the virtual home visit. Study staff will review the consent forms with participants via videoconferencing and will ask participants to sign the consent form (if deciding to participate) during the virtual home visit. Study staff will request that participants show their signature on the consent form to obtain visual confirmation of written informed consent. Study staff will document the date

and time that written informed consent is obtained during the virtual home visit. Participants will be provided with a self-addressed, postage paid envelope to return the consent form to the research office. Study staff conducting the virtual home visit and obtaining informed consent will sign and date the consent form upon return to the research office. Participants will also have the option of scanning their consent form and submitting it via email.

- According to our protocol, home visits are intended to be completed within 8 weeks of the baseline stress test. We will allow participants to enroll in Phase 2 of the study if their home visit (in-person or virtual) must be completed outside of this window.
- Scheduled exercise stress tests conducted at the outpatient cardiology clinic will be canceled until **5/30/2020**. Stress tests will be rescheduled when it has been determined to safe to resume in-person research activities. As a result, we will permit participants to complete exercise stress tests outside of the normal window (i.e., Week 22).
- Follow-up exercise stress tests that cannot be completed within 3 months of the end of the normal window due to the COVID-19 pandemic and clinical research restrictions will not be (re)scheduled. Participants will receive partial compensation for completing other research activities at this assessment period. Affected participants will be notified of this change by study staff via telephone or other method of communication used to contact participants during the course of the study.
- Participants who have provided verbal consent to participate in Phase 1 and who have completed the baseline questionnaires, but whose Phase 1 stress tests have been cancelled, will receive partial compensation for their time and effort. Additionally, we will ask these participants to complete the baseline questionnaire again when in-person research activities resume and their stress tests are rescheduled. Participants will

receive full compensation for participating in Phase 1 if the questionnaire and other study activities are completed, meaning that participants will be compensated for both completed administrations of the baseline questionnaire. These procedures are necessary to ensure that the questionnaire data reflects the same timeframe as data obtained from the exercise stress test.

The above modifications will be in effect when necessary as indicated by clinical research guidelines issued by NCH, including the Research Institute and Center for Biobehavioral Health. The standard protocol will apply when no clinical research restrictions are in place, or when the provisions in the modified protocol are not applicable to the participant/study activity. The above modifications will be documented for all affected participants, and we will report these deviations to the IRB and DSMB in the context of routine continuing reviews and safety meetings, respectively.

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