PROTOCOL TITLE:

The SPROUT (pilot) project: Starting pregnancy with robustness for optimal upward trajectories

PROTOCOL VERSION/AMENDMENT # AND DATE

Protocol Version 2 (7/20/2020)

PRINCIPAL INVESTIGATOR:

Erin Wentz, PT, PhD

1.0 Objectives

1.1 Describe the purpose, specific aims, or objectives of this research. Specifically, explain why it is important to do the study.

Historically, pregnant women were advised to refrain from exercise due to concerns of maternal and fetal risk such as preterm delivery, low infant birth rate and fetal stress. Despite current research that has demonstrated substantial benefits for maternal, fetal, and infant health, only 9-15% of pregnant women meet the current physical activity recommendations.[1-3] In addition, pregnancy exercise research is confounded by a lack of randomized controlled trials (RCT) that include diversity in participant demographics, specifically inner city populations, and difficulty accurately quantifying weekly exercise volume. We propose a pilot RCT investigating two different approaches to exercise intervention across a spectrum of demographics that we believe will result in improved exercise adherence as well as in maternal and infant health outcomes.

1.2 State the hypothesis to be tested, if applicable.
NOTE: A hypothesis is a specific, testable prediction about what you expect to happen in your study that corresponds with your above listed objectives.

Specific Aim #1: To determine the feasibility of two types of exercise interventions (supervised & home exercise) in terms of design, implementation and adherence. Our working hypothesis is that both supervised and home exercise interventions will be implementable as designed in pregnant women as evidenced by recruitment, eligibility, retention, follow-up and exercise adherence from 1st trimester through 6-months post-natal at a 60% rate, but that adherence to the two types of exercise interventions will differ by demographic. A secondary exploratory hypothesis is that we will be able to successfully recruit and retain 50% of our pregnant women from the Syracuse Community Health Center (primarily women with lower resources).

Specific Aim #2: To determine the appropriateness of the outcome measures proposed for the exercise intervention in detecting changes in maternal aerobic fitness, quality of life (QOL), fatigue, sleep quality, depression, and weight change throughout pregnancy and 6-months post-natal as measured by the Balke Ware submaximal test; SF-12 Generic Quality of Life (QOL); Multidimensional Fatigue Inventory (MFI); Pittsburgh Sleep Quality Index (PSQLI); Center for Epidemiologic Studies Depression Scale (CES-D); Edinburgh Postnatal Depression Scale (EPDS); and the Pregnancy Physical Activity Questionnaire (PPAQ). Our working hypothesis is that the above outcome measures will be able to detect changes in maternal outcome measures in both exercise groups.

2.0 Scientific/Safety Endpoints

2.1 Describe the scientific endpoint(s), the main result or occurrence under study. NOTE: Scientific endpoints are outcomes defined before the study begins to determine whether the objectives of the study have been met and to draw conclusions from the data. Include primary and secondary endpoints. Some example endpoints are: reduction of symptoms, improvement in quality of life, or survival. Your response should not be a date.

The scientific endpoint of this project is determining if the study is feasible in terms of the proposed approach and if the planned outcome measures are appropriate for detecting change in the maternal dependent variables in all three participant groups.

3.0 Background

3.1 Provide the scientific or scholarly background, rationale, and significance of the research based on the existing literature and how it will contribute/fill in gaps to existing knowledge.

Physical activity during pregnancy has substantial benefits for maternal and fetal health including: reduced risk of excessive weight gain, developing pre-eclampsia (PE), gestational diabetes mellitus (GDM) and gestational hypertension (GH), pre-term birth, macrosomia; depressive symptoms, and developing childhood obesity; and, can improve maternal sleep; and neonatal neuromotor skills at 1-month of age.[4-18] Despite the fact that African American women are two times more likely to have a pre-term delivery, have a higher pre-pregnancy body mass index (BMI) than Caucasian women and have a higher obesity rate, non-Caucasian pregnant women are less likely to engage in exercise and participate in more sedentary activity compared to Caucasian pregnant women.[19-22] Therefore, interventions that increase exercise adherence in a prescription that is achievable and sustainable for pregnant women across a wide demographic is of critical importance for optimal maternal and neonatal outcomes.

Evidence suggests that cardiovascular exercise performed at moderate intensity starting in the first trimester and continuing until birth is not associated with an increased risk for preterm birth (<37 weeks)

or low birth weight, even in previously sedentary women; and, does not compromise maternal or fetal health as assessed by mean gestational age, type of delivery, incidence of preterm delivery, birthweight, neonatal head circumference, Apgar score or neonatal complications.[23-24] A major benefit of exercise during pregnancy is assistance with weight control since excessive weight gain and inactivity are a risk factor for pregnancy complications including GDM, GH, and macrosomia.[25-26] Modest increases in maternal BMI beyond standard ranges are associated with increased risk of stillbirth and neonatal, perinatal and infant death.[27-28] Furthermore, pre-natal exercise has been associated with a reduction in pre- and post-natal depression with some evidence for improvement in sleep quality, fatigue, and quality of life. [12,18, 29-31]

Besides being associated with higher Apgar scores, exercise during pregnancy has been linked to decreased risk for childhood obesity and has been demonstrated to increase serum growth factors in neonates which may have beneficial implications for brain health and cognitive performance in the developing fetus. [14,32-34] Infants of mothers who exercised during pregnancy demonstrated higher neuromotor abilities at 1-month of age than infants of mothers who did not exercise.[14] Therefore, in order to minimize negative health prenatal outcomes and to maximize beneficial health outcomes in the pre and post-natal period, it is imperative that we discover how to promote participation and adherence to an appropriate pre-natal exercise intervention across a spectrum of demographics.

3.2 Include complete citations or references:

Literature cited

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4.0 Study Design

4.1 Describe and explain the study design (e.g. case-control, cross-sectional, experimental, interventional, longitudinal, and observational). Indicate if there is randomization, blinding, control group, etc. If randomizing, explain how this will be

achieved. For studies that have a complex study design (i.e., multiple arms and treatments), include a schematic diagram.

This is a pilot investigation (feasibility) of a future larger study of interventional design with randomization. Participants in the pilot phase of the project will be randomized using a free online research randomizer (randomizer.org).

5.0 Data Management and Analysis

5.1 Describe the data analysis plan, including any statistical procedures. This section applies to both quantitative and qualitative analysis.

Statistical analysis used to determine feasibility of the exercise intervention will include general descriptive statistics to assess recruitment, eligibility, retention, follow-up and exercise adherence. In addition, we will conduct a survey and interview of subjects related to acceptability to participate in EX and HOMEEX and discuss barriers to regular exercise which will be analyzed using descriptive statistics and a phenomenological approach. To determine the feasibility of maternal and infant outcomes, Kruskal-Wallis and Friedman's ANOVA will be used to investigate between group and within group differences. Relationships between variables will be analyzed using Spearman correlation coefficient. Because this is a feasibility study, the results will be used as preliminary data to apply for future funding and also will provide variable quantitative and qualitative data for validating interventions that can increase adherence to exercise guidelines during pregnancy in women with different ethnic and socioeconomic backgrounds.

5.2 If applicable, provide a power analysis for the number of subjects to be included. If qualitative research, so state, and provide general justification for the total number of subjects proposed.

NOTE: This may not apply to certain types of studies, including chart/records reviews, survey studies, or observational studies. This question is asked to elicit whether the investigator has an adequate sample size to achieve the study objectives and justify a conclusion.

This is a pilot project aimed to investigate feasibility of approach and appropriateness of maternal outcome measures. If the working hypotheses are supported, the next phase will be a large, randomized intervention study. Pilot data from this project can be utilized in the power analysis for the larger study.

6.0 Local Number of Subjects

6.1 Indicate the total number of subjects who will be enrolled or records that will be reviewed through Upstate.

No more than 18 total participants (six per group)

6.2 If applicable, indicate your screen failure rate, i.e., how many subjects you expect to screen to reach your target sample.

54 (anticipate that for every three women screened, one will participate in the study)

6.3 Justify the feasibility of recruiting the proposed number of eligible subjects within the anticipated recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?

The feasibility of recruitment is part of what is being investigated in this pilot project and findings from this project will inform the recruitment plan of the future large intervention study. The plan for the pilot is to recruit no more than 18 (six per group) low risk pregnant women with a singleton pregnancy from Syracuse Community Health Center (50%), University OB/GYN Associates, and Upstate Community OB/GYN. All women will be enrolled during the 1st trimester (6 to 13-weeks' gestation) and without absolute contraindications to moderate intensity exercise during pregnancy as defined by American College of Sports Medicine (ACSM) and American College of Obstetricians and Gynecologists (ACOG). [44-45] All participants will be cleared for exercise by their OB/GYN.

7.0 Inclusion and Exclusion Criteria

7.1 Describe, in bullet points, the criteria that define who will be included in this study:

- Adult pregnant women (i.e. 18 years of age and older)
- Low risk, singleton pregnancy
- In first trimester of pregnancy (6 to 13 weeks gestation)
- Without absolute contraindications to moderate intensity exercise during pregnancy as defined by the American College of Obstetricians and Gynecologists
- Exercise clearance from OB/GYN

7.2 Describe, in bullet points, the criteria that define who will be excluded from this study:

- Pregnancies greater than low risk for any reason
- Pregnant with more than one fetus
- Absolute exercise contraindications and/or lack of exercise clearance from OB/GYN

7.3 Indicate whether you are specifically recruiting or targeting any of the following special populations in your study using the checkboxes below.

☐ Adults unable to consent (*complete and upload Supplemental Form A)*

☐ Minors (under 18 years old)

☒ Pregnant women

☐ Prisoners

6.4 Indicate if you will include minorities (American Indians, Alaskan Native, Asian, Native Hawaiian, Pacific Islander, Black [not of Hispanic origin] and Hispanic) as Federal mandates require that you include minorities unless you can justify their exclusion

☒ Yes

☐ No, Justify:

8.0 Vulnerable Populations

8.1 For research that involves pregnant women, review, complete and upload Supplemental Form B: Research Involving Pregnant Women, Fetuses, or Neonates.

☒ Confirmed

☐ N/A: This research does not involve pregnant women.

8.2 For research that involves neonates of uncertain viability or non-viable neonates, review, complete and upload Supplemental Form B: Research involving Pregnant Women, Fetuses, or Neonates.

☐ Confirmed

☒ N/A: This research does not involve non-viable neonates or neonates of uncertain viability.

8.3 *For research that involves prisoners, review, complete and upload Supplemental Form C: Research involving Prisoners*

☐ Confirmed

☒ N/A: This research does not involve prisoners.

8.4 For research that involves minors (under 18 years), review, complete and upload Supplemental Form D: Research involving Minors

☒ Confirmed

☐ N/A: This research does not involve minors (under 18 years),

8.5 Consider if other specifically targeted populations such as students, employees of or educationally or economically disadvantaged persons are vulnerable. Provide information regarding their safeguards and protections, including safeguards to eliminate coercion or undue influence.

☒ N/A

9.0 Eligibility Screening

9.1 *Describe screening procedures for determining subjects' eligibility. Screening refers to determining if prospective participants meet inclusion and exclusion criteria. Include (upload) all relevant screening documents with your submission (e.g. screening protocol, script, questionnaires).*

Protocol: Interested pregnant women (responding to internet requests for participants or posted flyers) will be contacted by phone or email to answer questions about the study and to verify eligibility for the study (i.e. inclusion, exclusion criteria). Participants that are interested in registering for the study will be required to get exercise clearance from their OB/GYN before being randomized into one of the three groups and then beginning that group's exercise protocol.

Clearance for participation must be provided by the participant's OB/GYN (not primary care physician or non-physician providers)

☐ N/A: There is no screening as part of this protocol.

10.0 Recruitment Methods

☐ N/A: Subjects will not be recruited.

10.1 Describe source of subjects: When, where, and how potential subjects will be recruited.

NOTE: Recruitment refers to how you are identifying potential participants and introducing them to the study; for example, physician referral, database search, reviewing medical records, research participant groups/help/advocacy groups, advertising companies, call centers, in person announcements / presentations, etc.

Participants will be recruited via physician referral, posted flyers and internet postings (e.g. local mom's groups, Upstate announcements, Department of Physical Therapy Education Facebook page, etc)

10.2 Describe how you will protect the privacy interests of prospective subjects during the recruitment process.

NOTE: Privacy refers to an individual's right to control access to him or herself. This is NOT asking about confidentiality of data.

All screening and information exchanges with prospective participants will happen in private (in a one on one setting).

10.3 Identify all materials that will be used to recruit subjects and upload copies of these documents (such as telephone scripts, flyers, questionnaires, posters, letters, e-mails, pamphlets, advertisements).

Flyers, e-mails

11.0 Research Methods & Procedures

Provide a detailed description of the methods and procedures that will be used to carry out the study. Include a summary of study visits and procedures (i.e., schedule of events table) in the space below or as an attachment.

Please make sure to include:

- Dosing of drugs and other details of study drug administration and study treatments
- A list and description of any experimental procedures
- A list and description all tests & procedures that would no be done if the subjects were not in the study
- An explanation how study participation differs from the standard of care
- Procedures being performed to monitor subjects for safety or to minimize risks

Eighteen low risk pregnant women with a singleton pregnancy will be recruited for this pilot project from Syracuse Community Health Center (50%), University OB/GYN Associates, and Upstate Community OB/GYN. All women will be enrolled during the 1st trimester (6 to 13-weeks' gestation) and without absolute contraindications to moderate intensity exercise during pregnancy as defined by American College of Sports Medicine (ACSM) and American College of Obstetricians and Gynecologists (ACOG). [44-45] All participants will be cleared for exercise by their OB/GYN. The ACSM and ACOG guidelines include 150 min/wk of cardiovascular activity at a moderate intensity; 2-3 days/week of resistance training; and 2-3 days/wk of flexibility training.[44-45] Clearance will come exclusively from the OB/GYN.

Women will be randomly assigned to either UA, EX or HOMEEX. Women randomized to EX will attend three exercise classes/week at the Institute for Human Performance (IHP) and given flexibility to attend classes between the hours of 7:30a-6p, Mon-Fri. Each session will consist of: 5-min flexibility warm-up and cool-down; 40 min of moderate intensity calculated as 40-59% Heart Rate Reserve (HRR) along with Rating of Perceived Exertion (RPE) between 13-14; and 20 minutes of resistance with an additional 30 minutes of unsupervised home aerobic activity per week. The women will be given their choice of aerobic equipment or walking either track/ treadmill to achieve a total of 40 minutes of moderate intensity exercise.

Women assigned to HOMEEX will receive instructions for their home walking program including tips for walking indoors and outdoors, exercise handouts for warm-up/cool-down activities, demonstrations for resistance training activities and an exercise log. HOMEEX women will be contacted twice per week to discuss their progress, barriers/challenges faced, ask questions, and strategies to achieve the exercise guidelines. If women in either EX or HOMEEX are unable to achieve 30-40 minutes of continuous aerobic exercise at the start of the study, they will be given an individualized, progressive exercise program that breaks activity into smaller 10 minute sessions and/or increases rest between sessions to achieve the 150 minutes/week of moderate intensity activity.

Both exercise groups will receive exercise counseling during their first meeting in addition to materials on the benefits of exercise, a log to record additional activity completed each week, goal setting, making time for exercise/making exercise a habit and exercise behavioral strategies. The UA group will receive an exercise log to record any weekly activity in addition to a weekly phone call/text/email to remind the individual to download information from the Polar Ignite watch (Bethpage, NY) and a reminder to complete the weekly exercise log.

Each woman enrolled in the study will be given a Polar Ignite watch to wear for the study duration. This monitor will be programmed for moderate intensity HRR and will alarm if HR falls above/below during exercise for both exercise groups. In addition, the monitor will record all other activity within the HRR range and will be used to verify information obtained from activity and QOL questionnaires to reduce self-reported bias in all groups. For the control group, the watch will record activity by HR intensity level that can be quantified on a weekly basis.

Regardless of randomization, all women will report to the IHP between weeks 11-13 (late 1st trimester) for baseline testing and to review past medical history, medications and exercise history. Height will be measured to the nearest 0.25 inch using a stadiometer and converted to meters. BMI will be calculated using the self-reported pre-pregnancy weight. Gestational weight gain will be calculated from subtracting the pre-pregnancy weight from weight at the last obstetrics visit prior to delivery. All women will also perform a submaximal Balke-Ware

submaximal treadmill test to determine HRR for the two exercise groups and estimate VO_2max using the Pollock equation which will be repeated at 3- and 6-months after birth to compare aerobic fitness levels.[46]

All women will complete the following questionnaires at baseline (late 1st trimester), 25-26 weeks (late 2nd trimester), and 37-38 weeks (late 3rd trimester), and monthly through 6-months post-natal: MFI, SF-12 QOL; PSQLI; CES-D; EPDS; and the PPAQ. All questionnaires have been demonstrated to have good validity, reliability, and internal consistency and the CES-D and EPDS are similar to each other in regards to internal consistency and test-retest reliability.[47-57]

Infants from mothers in all three groups will have their gross and fine motor, and cognitive development measured monthly (months 1-6) at home using the Bayley Scales of Motor Development, 4th edition.[58] The Bayley 4 is a standardized, norm-referenced tool with subtest level scaled scores, domain level composite scores, percentile ranks, and developmental age equivalents.[58] Infant height and weight will be measured monthly through 6-months of age.

Women assigned to EX will have all of their supervised pregnancy exercise sessions, questionnaires, and weight measured at the IHP. After delivery, women assigned to EX will resume their supervised IHP exercise program between 4-8 weeks (depending on delivery mode) when they are cleared for activity by their physician, complete exercise testing at 3- and 6-months and will have monthly home visits for infant testing through 6 months. HOMEEX and UC women will visit the IHP at baseline, 3 & 6-months post-delivery for exercise testing, questionnaires, and weight measurement. HOMEX and UC groups will receive home visits for: 2nd & 3rd trimester questionnaires and weight measurement and every month post-delivery for questionnaires, weight measurement and infant testing.

Statistical analysis used to determine feasibility of the exercise intervention will include general descriptive statistics to assess recruitment, eligibility, retention, follow-up and exercise adherence. In addition, we will conduct a survey and interview of subjects related to acceptability to participate in EX and HOMEEX and discuss barriers to regular exercise which will be analyzed using descriptive statistics and a phenomenological approach. To determine the feasibility of maternal and infant outcomes, Kruskal-Wallis and Friedman's ANOVA will be used to investigate between group and within group differences. Relationships between variables will be analyzed using Spearman correlation coefficient. Because this is a feasibility study, the results will be used as preliminary data to apply for future funding and also will provide variable quantitative and qualitative data for validating interventions that can increase adherence to exercise guidelines during pregnancy in women with different ethnic and socioeconomic backgrounds.

In order to monitor the safety of the participants, all exercise performed by the EX, HOMEXX, and UC groups will follow ACSM and ACOG guidelines for moderate-intensity cardiovascular and resistance exercise. In addition, all women will wear a Polar Ignite watch that will alarm if their HR exceeds moderate level intensity. All women in the EX will be supervised during their exercise sessions. Women in the HOMEEX group will be meet individually with either Dr. Wentz or Dr. Sames to discuss safe exercise principles. They will be given written information on exercising in a moderate intensity range for both cardiovascular and resistance exercise. In addition, they will be contacted twice per week to discuss their program and any questions about exercise. Lastly, their HR data will be downloaded and analyzed to confirm that they are exercising in a moderate intensity rate. Women in the UC group will be told to continue participating in whatever activity they are currently engaged. They will be given an activity log to record their activity and we will download their HR data.

11.1 Describe what data, including long-term follow-up, will be collected.

NOTE: For studies with multiple data collection points or long-term follow up, consider including a schedule or table in your response.

Instruments being utilized in this study:

- The Bayley Scales of Infant Development, 4th edition
- Physical Activity diary
- Pregnancy Physical Activity Questionnaire
- Short-Form 12 (SF-12) Health survey
- Pittsburgh Sleep Quality Index
- Multidimensional Fatigue Inventory
- Edinburgh Post-Natal Depression Scale
- Center for Epidemiologic Studies Depression Scale

Activity		2020 September to December	2021 January to April	2021 May to August	2021 September to December	2022 January to April	2022 May to June
Recruitment (6 UC, 6 EX, 6 HOMEEX)		X					
Maternal Interventions		X	X	X	X	X	
Maternal Baseline Measurements		X	X				
Maternal Prenatal Measurements		X	X	X			
Maternal Post Natal Measurements				X	X	X	
Infant Measurements				X	X	X	X
Data Analysis					X	X	
Dissemination of results							X
First publication submission						X	
Target grant submission							X

List, and upload, any instruments or measurement tools used to collect data (e.g. survey, scripts, questionnaire, interview guide, validated instrument, data collection form).

11.2 Describe any source records that will be used to collect data about subjects (e.g. school records, electronic medical records).

n/a

11.3 Describe whether individual subject results (such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject's primary care physicians) and if so, describe how it will be shared.

Participants will have access to the results of their testing immediately if requested but a summary of information will be provided to each participant at the end of their participation in the study.

Participants will independently choose if they wish to share any of their results with their primary care physician/OB/GYN

11.4 Indicate whether or not generalized study results will be shared with subjects or others, and if so, describe how these will be shared.

Overall (generalized) study results will be shared with participants at the completion of the study via an electronic and/or hard copy summary of results/findings.

12.0 Study Timelines

12.1 Describe the anticipated duration of the study needed to enroll all study subjects.

The plan is to enroll all study participants in three months.

12.2 Describe the duration of an individual subject's participation in the study. Include length of study visits, and overall study follow-up time.

Each participant's time in the study will be 15 months +/- 4-8 weeks (depending on what point in the first trimester a participant begins)

12.3 Describe the estimated duration for the investigators to complete this study (i.e. all data is collected and all analyses have been completed).

The time from first recruitment to wrap up of this phase of the project is estimated to be 22 months.

13.0 Research Setting

13.1 Describe all facilities/sites/locations where you will be screening and conducting research procedures. Include a description of the security and privacy of the facilities (e.g. locked facility, limited access, privacy barriers). Facility, department, and type of room are relevant. Do not abbreviate facility names.

Example: "A classroom setting in the New Academic Building equipped with a computer with relevant survey administration software", "The angiogram suite at University Hospital downtown campus", The Clinical Research Unit in the Institute for Human Performance."

The second floor of the Institute for Human Performance (private room as needed for evaluation and/or exercise prescription and the physical therapy gym); individual participant's homes

13.2 For research procedures being conducted, for this study, external to Upstate (e.g., in schools, out-of-state, internationally, etc.) describe:

- *Site-specific regulations or customs affecting the research*
- *The composition and involvement of any community advisory board*
- *Local scientific and ethical review structure outside the organization.*
- *Local issues affecting the research and rights of research subjects.*

NOTE: This question is not referring to multi-center research. If this research is being conducted internationally, Supplemental Form E must be completed and uploaded.

☒ N/A: This study is not conducted outside of Upstate.

14.0 Resources and Qualifications

14.1 The Principal Investigator (PI) must confirm, in consultation with Chair and Dean as applicable, that adequate resources are present to conduct and complete the study compliantly and safely. Specifically:

- *The proposed subject population(s) are available in sufficient numbers to meet the study requirements*
- *Sufficient funds are available to conduct and complete the study compliantly and safely*
- *The PI and study team have sufficient time to conduct and complete the study compliantly and safely*
- *The PI has determined that the named study team is qualified to conduct the research compliantly and to monitor the safety and welfare of the enrolled research subjects effectively*
- *The PI ensures that the study team is fully aware of his/her involvement in this study and the details of the study protocol*
- *The PI ensures that the study teams will only be involved in research procedures for which they have been trained, and are currently certified and/or licensed, if required.*

☒ **Confirmed**

14.2 Describe the availability of medical or psychological resources that subjects might need as a result of anticipated consequences of the research, if applicable. (e.g, "on-call availability of a counselor or psychologist for a study that screens subjects for depression").

Each participant's OB/GYN and their emergency care contact will be immediately contacted in the event of any adverse events.

14.3 Describe your process to ensure that all study team members are updated on the progress of the research and the regulatory requirements (including enrolled subjects, unanticipated problems etc.)

Dr. Wentz and Dr. Sames will be supervising the EX subjects training, fitness testing, collection of questionnaires in addition to the weekly contact of the HOMEEX subjects. In addition, Dr. Wentz and Dr. Sames will be conducting all follow-up testing and home visits. Upstate DPT students and *Vitality* Fitness staff members will be used to help with the supervision of the EX subjects and testing of the EX, HOMEEX, and UC groups. Since Dr. Wentz and Dr. Sames are directly supervising and testing subjects in this study, they will be aware of the research progress and any unanticipated problems which can be conveyed to the DPT students and *Vitality* Fitness staff. Any individuals assisting in the conduct of the study will be added to the registration form.

15.0 Provisions to Protect the Privacy Interests of Subjects

15.1 Describe how you will protect subjects' privacy interests during the course of the research and any steps you will take to make the subject feel at ease.

NOTE: Privacy refers to an individual's desire/right to control access to or to place limits on whom they interact with or whom they provide personal information. Privacy applies to the person. Confidentiality refers to how data collected about individuals for the research will be protected by the researcher from release. Confidentiality applies to the data.

Examples of appropriate responses include: "participant only meets with a study coordinator in a private office setting where no one can overhear", or "the participant is reminded that they are free to refuse to answer any questions that they do not feel comfortable answering."

Participants will only be evaluated in a private office setting where no one can overhear and they will also be able to request that exercise sessions occur in a similar private setting if that is their preference. Participants will be reminded that they are free to refuse to answer any questions that they do not feel comfortable answering.

16.0 Confidentiality

A. Confidentiality/Security of Study Data

Describe the local procedures for maintenance of security and confidentiality of **study data and any records that will be reviewed for data collection.**

16.1 Where and how will all data and records be stored? Include information about: password protection, encryption, physical controls, authorization of access, certificates of confidentiality, and separation of identifiers and data, as applicable. Include physical (e.g. paper) and electronic files.

All paper data collection files will be stored in a locked credenza located in Room 2016 of the IHP (Dr. Sames office). This office is locked with key access held by Dr. Sames and Amy Allen

(*Vitality* Fitness staff member). All demographic, testing, questionnaire, and exercise data will be electronically stored on the Shared T drive (CR1\app2\Shared\Vitality) in a separate folder which is password protected. Data will be entered into the Shared by Dr. Wentz, Dr. Sames and *Vitality* Fitness staff member Amy Allen.

16.2 How long will the data be stored?

There is no scheduled date at which this information will be destroyed or no longer used. Because this information is a feasibility study, we will continue to use this study to apply for future grants and could be used for and it is not possible to determine when this will be complete.

16.3 Who will have access to the data?

Dr. Wentz, Dr. Sames

16.4 Who is responsible for receipt or transmission of the data?

Dr. Sames

16.5 How will the data be transported/transmitted?

na

B. Confidentiality of Study Specimens

Describe the local procedures for maintenance of confidentiality of study specimens.

☒ **N/A:** No specimens will be collected or analyzed in this research.
(Skip to Section 17.0)

16.6 Where and how will all specimens be stored? Include information about: physical controls, authorization of access, and labeling of specimens, as applicable.

16.7 How long will the specimens be stored?

16.8 Who will have access to the specimens?

16.9 Who is responsible for receipt or transmission of the specimens?

16.10 How will the specimens be transported?

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

☒ **N/A:** This study is not enrolling subjects OR is limited to records review procedures only OR is a minimal risk study

17.1 Describe the plan to evaluate the data periodically regarding both harms and benefits to determine whether subjects remain safe. The plan might include establishing a data safety monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor.

17.2 Describe what data are reviewed, including safety data, untoward events, and efficacy data.

17.3 Describe any primary or secondary safety endpoints.

17.4 Describe how the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).

17.5 Describe the frequency of safety data collection, including when safety data collection starts.

17.6 Describe who will review the safety data.

17.7 Describe the frequency of review of cumulative safety data.

17.8 Describe the statistical tests for analyzing the safety data to determine whether harm is occurring.

17.9 Describe any conditions that trigger an immediate suspension of the research.

18.0 Withdrawal of Subjects

☐ N/A: This study is not enrolling subjects. This section does not apply.

18.1 Describe anticipated circumstances under which subjects may be withdrawn from the research without their consent.

Failure to take part in scheduled visits without notification AND failure to respond to attempts at contact.

18.2 Describe any procedures for orderly termination.
NOTE: Examples may include return of study drug, exit interview with clinician. Include whether additional follow up is recommended for safety reasons for physical or emotional health.

n/a

18.3 Describe procedures that will be followed when subjects withdraw from the research, including retention of already collected data, and partial withdrawal from procedures with continued data collection, as applicable.

If a subject withdrawals from the study, their data will be included in the study up to the point of withdrawal.

18.4 Describe what will happen to data already collected.

Data that has already been collected will be stored physically and electronically as stated previously.

19.0 Risks to Subjects

19.1 In your opinion, what is the overall risk (physical and nonphysical) to research subjects in this study (minimal, greater than minimal or unknown)

minimal

19.2 Describe if any subjects are withdrawn from therapeutic procedures or drugs (e.g., washout periods) prior to, or during, their participation in the study.

N/A

19.3 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to their participation in the research. Consider physical, psychological, social, legal, and economic risks. Include a description of the probability, magnitude, duration, and reversibility of the risks.

NOTE: Breach of confidentiality is always a risk for identifiable subject data.

If a woman has been sedentary she may experience muscle soreness from participation in the exercise program that will dissipate after 4-7 days of regular exercise. In addition, a previously sedentary woman may experience initial fatigue (lasting 1 to 2 days) which will also dissipate within 4-6 weeks of consistent exercise. Participation in this research has minimal risks to the mother and fetus and all participants will be instructed as to what constitutes adverse responses and when to not engage in exercise. For mothers in the structured exercise group (EX), transportation to the IHP may be inconvenient and/or difficult. Following delivery, it may be more difficult for mothers to engage in the exercise program (HOMEX and EX) if they don't have childcare.

19.4 Describe procedures performed to minimize the probability or magnitude of risks, including procedures being performed to monitor subjects for safety.

All exercise performed by the EX, HOMEXX, and UC groups will follow ACSM and ACOG guidelines for moderate-intensity. In addition, all women will wear a Polar Ignite watch that will alarm if their HR exceeds moderate level intensity. All women in the EX will be supervised during their exercise sessions. Women in the HOMEEX group will be meet individually with either Dr. Wentz or Dr. Sames to discuss safe exercise principles. They will be given written information on exercising in a moderate intensity range for both cardiovascular and resistance

exercise. In addition, they will be contacted twice per week to discuss their program and any questions about exercise. Lastly, their HR data will be downloaded and analyzed to confirm that they are exercising in a moderate intensity rate. Women in the UC group will be told to continue participating in whatever activity they are currently engaged. They will be given an activity log to record their activity and we will download their HR data.

All women will be told that during exercise they may experience adverse changes including: abnormal blood pressure; fainting; and disorders of heart rhythm that can be minimized by stopping their exercise and immediately informing their physician of any unusual symptoms. In addition, they will be told to maintain their exercise intensity at a moderate level (conversational level) throughout each and all exercise sessions.

At the beginning and throughout the study, participants will be reminded that their participation is voluntary and they can stop participating in the study at any time.

With the exception of the depression questionnaires, the information being asked of participants is not sensitive information—e.g. how is your sleep, activity, fatigue and QOL? Participant information is confidential, not shared, securely kept, and coded by number.

While we will not be analyzing the data (e.g. results of depression or other questionnaires) during the study to avoid compromising interactions (e.g. bias) with participants, study personnel will be speaking to participants in the HOMEEX and EX groups multiple times per week. Participants will be asked about their next OB/GYN appointment and if anything about their health status has changed (this helps to also insure that each participant is maintaining an active relationship with her OB provider). The physician approval form that provides a participant with clearance to participate in the study will include a statement that asks the physician to inform study personnel immediately if the participant develops any contraindication, relative or absolute, to participation in an exercise program (e.g. fetal growth restriction or gestational hypertensive disorder). Gestational diabetes mellitus (GDM) will be handled per individual participant's OB/GYN recommendations. If a participant develops an absolute contraindication to participation in the study, they will be removed from the study. If a participant experiences an adverse event, a new clearance must be provided by OB/GYN for the participant to return to the study. In the case of an emergency, participants will be advised to seek care at Upstate Community Hospital. If a participant needs NICU care, they will be advised to seek care at Crouse or St. Joseph's hospital.

Only full term infants (birth at 37+ weeks gestation) will go on to participate in the neonatal portion of the study. Infants participating in this portion of the study will undergo monthly height, weight, motor and cognitive assessments that pose minimal to no risk to the infant. In the

event, that an assessment uncovers unexpected information (e.g. loss of weight, significantly delayed motor development), participants will be advised to contact their pediatrician.

Participants will regularly be asked how they are feeling. If a participant expresses that she is feeling blue or is having depressive thoughts, study personnel will recommend that she contact her health provider. We will follow up each week to check the status of these symptoms and to make sure they have spoken with their health provider. Participants in the control group are also being contacted weekly, so relationships are being established, and the same process for experiencing undesirable thoughts or feelings would apply.

19.5 If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable.

n/a

19.6 Indicate which research procedures, if any, may have risks to an embryo or fetus should the subject be or become pregnant.

☒ **N/A**

19.7 If you responded to 19.6 that there are such risks, how will you minimize the risk of a pregnancy occurring during the course of the study? (Select all that apply)

- ☐ Counseling on birth control and /or abstinence
- ☐ Pregnancy test during the study
- ☐ Pregnancy test prior to initiation of the study
- ☐ Other _____
- ☐ **N/A**

19.8 If applicable, describe possible risks to others who are not subjects.

n/a

20.0 Potential Benefits to Subjects

20.1 Describe the potential benefits that individual subjects may experience by taking part in the research. Include the probability, magnitude, and duration of the potential benefits.

For pregnant women, regular exercise has been associated with a reduced risk of maternal and fetal health including: reduced risk of excessive weight gain, developing pre-eclampsia (PE), gestational diabetes mellitus (GDM) and gestational hypertension (GH), pre-term birth, macrosomia; depressive symptoms, and developing childhood obesity; and, can improve maternal sleep; and neonatal neuromotor skills at 1-month of age. Adopting a sedentary lifestyle, has greater negative consequences on both maternal and neonatal health. Benefits of exercise last a lifetime and have both primary and secondary risk reduction of CVD, the number one killer of adults.

20.2 Indicate if there is no direct benefit.
NOTE: Compensation cannot be stated as a benefit.

Indicate if there is a potential benefit to others, future science or society.

Future science and practice for optimal maternal, fetal and neonatal outcomes during and after pregnancy.

21.0 Compensation for Research-Related Injury

X☐

21.1 If the research procedures carry a risk of research related injury, describe the available compensation to subjects in the event that such injury should occur.

In the event of a research related injury, treatment is available at University Hospital but is not free of charge. The costs will be billed to the participant and/or the participant's insurance company. SUNY Upstate Medical University has no funds set aside to compensate for injuries.

22.0 Economic Burden to Subjects

22.1 Describe any costs that subjects may be responsible for because of participation in the research.
NOTE: Some examples include transportation or parking.

Parking stickers will be purchased so participants do not need to be reimbursed—participants will be given stickers when they come to IHP.

☐

N/A: This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

23.0 Compensation for Participation

☐ **N/A:** There is no compensation for participation. This section does not apply.

23.1 Describe the amount/nature and timing/scheduling of any compensation to subjects, including monetary, course credit, or gift card compensation. Describe any prorated payments based on participation.

Participants will be given parking stickers when they come to IHP when they have to park there for scheduled visits. If subjects do not have personal transportation, public transportation or private transportation costs from Uber or Lyft will be reimbursed. Additionally, subjects will receive $10 in appreciation for their time for each face to face visit. Payments will be made on the 15th of month for expenses incurred in the month prior.

24.0 Informed Consent

24.1 Will you be obtaining consent from subjects?

☒ ***Yes*** *(If yes, Provide responses to each question in this Section, and upload your consent documents)*

☐ ***No*** *(If no, Skip to next section)*

24.2 Describe how the capacity to consent will be assessed for all subjects. (See SOPs, section 14.7.2 for guidance)

The subject's ability to consent will be assessed by discussing the proposed study as presented in 24.3 and then asking them questions about the study including questions about randomization; requirements to participate in the study; ability to withdrawal from the study; and risks and benefits of participating in the study.

24.3 Describe the consent process that will be conducted to ensure that subject is fully informed regarding study details and subject rights. Include where the consent process will take place, with consideration of the need to protect the subject's right to privacy.

Subjects will meet individually in a private office (2016 IHP) where a discussion of the study requirements will be explained including the randomization process and requirements for each group; subject rights including withdrawal from the study; who will be looking at their protected health data; access to their health data and results; and risks and benefits of participating in the

study. After this brief discussion and a positive assessment of their ability to consent, subjects will be given the consent form and encouraged to read it in its entirety.

24.4 Describe the process to ensure that subjects are provided with sufficient time to consider taking part in the research study. Include whether there is any time period expected between informing the prospective subject and obtaining the consent.

NOTE: It is respectful to the prospective subject to ensure that sufficient time is given to have their questions answered and to consider their participation

Prospective participants will be supplied with a copy of the consent (electronic or hard copy) to review for several days before the first visit occurs. At the time of the first visit, the consent will be reviewed and questions will be answered before the participant is asked to sign the consent.

24.5 Describe the process to ensure ongoing consent, defined as a subject's willingness to continue participation for the duration of the research study.

Subjects will be informed during the consenting process that their participation is completely voluntary and that they may withdraw from the study at any time, for any reason, no questions asked. Any subjects express hesitancy or appear hesitant about continuing in the study after the initial consenting process with be counseled again about their ability to withdraw without repercussions of any type.

Non-English Speaking Subjects

☒ *N/A: This study will not enroll Non-English speaking subjects.*

24.6 Indicate which language(s) other than English are likely to be spoken/understood by the prospective study population or their legally authorized representatives.

24.7 If subjects who do not speak English will be enrolled, describe the process to consent the subjects, as well as the process to be used to ensure their understanding of research procedures throughout the conduct of the study. Review SOP's section 13.9.1 for important policies in this regard.

Response:

Adults Unable to Consent

☒ **N/A:** This study will not enroll adults unable to consent (go to next section).

24.8 Justify why it is necessary to include adult subjects who are unable to consent.

24.9 Describe how you will identify Legally Authorized Representatives (LAR) for the subjects that will be consistent with the NYS law (Review SOP's section 13.3)

Note: For research conducted outside of New York State, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the research.

24.10 Describe the process for obtaining assent from the adult subjects
Indicate whether assent will be obtained from all, some, or none of the subjects. If some, indicate which adults will be required to assent and which will not.

If assent will not be obtained from some or all subjects, provide an explanation of why not.

24.11 Describe whether assent of the adult subjects will be documented and the process to document assent.

24.12 Describe how you will obtain consent from a subject to use their data if they later become capable of consent. How will capacity to consent be assessed and by whom?

25.0 Waiver or Alteration of Consent Process

Complete this section if:

- Informed consent will not be obtained at all
- Informed consent will be obtained, but not documented, or

- consent will be obtained, but not all required information will be disclosed (e.g., in deception research)

☒ **N/A:** A waiver or alteration of consent is not being requested.

25.1 Review, complete, and upload Supplemental Form F: General Waiver or Alteration of Consent

☐ Confirmed

26.2 If the research involves a waiver of the consent process for planned emergency research, please contact the IRB Office for guidance regarding assistance in complying with federal regulations governing this activity (see SOPs section 13.12).

26.0 Multi-Site Research (Multisite/Multicenter Only)

☒ **N/A:** This study is not an investigator-initiated, multi-site study. This section does not apply.

26.1 If this is a multi-site study where Upstate is the lead site and/or the IRB of record, describe the processes to ensure communication among sites. Include:

- *All sites have the most current version of the IRB documents, including the protocol, consent document, and HIPAA authorization.*
- *All required approvals have been obtained at each site (including approval by the site's IRB of record).*
- *All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.*
- *All engaged participating sites will safeguard data as required by local information security policies.*
- *All local site investigators conduct the study appropriately.*
- *All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.*

26.2 Describe the method for communicating to engaged participating sites:

- *Problems*
- *Interim results*
- *Study closure*

*26.3 Indicate and statistically justify the total number of subjects that will be enrolled or records that will be reviewed **across all sites**.*

27.0 Banking Data or Specimens for Future Unspecified Use

☒ **N/A:** This study is not storing data or specimens for research outside the scope of the present protocol. This section does not apply.

27.1 If data will be banked (stored) for research outside of the scope of the present protocol, describe where the data will be stored, how long they will be stored, how will they be accessed, and who will have access to the data

NOTE: The response here must be consistent with the information provided to subjects in the Consent Documents

27.2 If specimens will be banked (stored) for research outside of the scope of the present protocol, describe where the specimens will be stored, how long they will be stored, identifiers that will be associated with each specimen, how will they be accessed, and who will have access to the specimens

NOTE: The response here must be consistent with the information provided to subjects in the Consent Documents

27.3 Describe the procedures to release banked data and/or specimens for future uses, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

28.0 Drugs and Devices

☒ **N/A:** This study does not involve drugs or devices. This section does not apply.

28.1 Does this study involve use of radiopharmaceuticals? ☐ Yes ☐ No

28.2 For investigational devices (including marketed devices being used off label & humanitarian use devices), Provide the following information:

- *Where will the device(s) be stored? Note that the storage area must be within an area under the PI's control*
- *Describe the security of the storage unit/facility*
- *Provide full detail regarding how the dispensing of the device(s) will be controlled (accountability of removal/return of used devices, and disposition of remaining devices at the conclusion of the investigation) and documented (accounting records/logs)*

28.3 For research including drugs (investigational and FDA approved). Complete and upload the Pharmacy Worksheet and supporting materials (IB's) and obtain Pharmacy approval and sign off.

☐ Confirmed
☐ **N/A:** This study does not involve drugs