NEW YORK STATE PSYCHIATRIC INSTITUTE

INSTITUTIONAL REVIEW BOARD

MEMORANDUM

May 25, 2018

TO: RICHARD P. SLOAN, PHD

FROM: Dr. Edward Nunes, Co-Chair, IRB

Dr. Agnes Whitaker, Co-Chair, IRB

SUBJECT: EXPEDITED APPROVAL OF PROTOCOL AMENDMENT

The amendment to your protocol #7466 entitled: THE ANTI-INFLAMMATORY EFFECTS OF EXERCISE AND PEANUT CONSUMPTION **(To use the Columbia RecruitMe platform for subject recruitment, as per the 5/10/2018 memorandum)** has been approved by the Psychiatric Institute - Columbia University Department of Psychiatry Institutional Review Board.

Please note that this does not change the IRB's cycle of review. A progress report and an application for continuing review will be required 2 months before the study's approval is due to expire: (4/30/2019).

Signed copy on file at IRB.
EN/AW/collins

Protocol Title:
The Anti-Inflammatory Effects of Exercise and Peanut Consumption

Version Date:
05/25/2018

Protocol Number:
7466

First Approval:
05/15/2017

Expiration Date:
04/30/2019

Contact Principal Investigator:
Richard Sloan, PHD
Email: rps7@columbia.edu
Telephone: 646-774-8940

Co-Investigator(s):
Martin Picard, PHD

Research Chief:
Richard Sloan, PHD

Cover Sheet

Choose ONE option from the following that is applicable to your study
If you are creating a new protocol, select "I am submitting a new protocol." As 5 Year Renewals are no longer required, this option remains for historical purposes.
I am proposing an amendment only to an existing protocol

Division & Personnel

Division

What Division/Department does the PI belong to?
Behavioral Medicine/Psychiatry
Within the division/department, what Center or group are you affiliated with, if any?
none

Unaffiliated Personnel

List investigators, if any, who will be participating in this protocol but are not affiliated with New York State Psychiatric Institute or Columbia University. Provide: Full Name, Degrees and Affiliation.

Wahida Karmally, Dr. PH RDN, CDE, CLS Director of the Bionutrition Research Core of the Columbia University Medical Center Irving Institute for Clinical and Translational Research and Associate Research Scientist and Lecturer in Dentistry at Columbia University

Amendment

Describe the change(s) being made
We would like to use the Columbia RecruitMe platform for subject recruitment.
Provide the rationale for the change(s)
We hope that this will increase our recruitment rates.
Comment on the extent to which the proposed change(s) alter or affect risks/benefits to subjects
N/A
Comment on if the proposed change(s) require a modification to the Consent Form (CF)
No.

Procedures

To create the protocol summary form, first indicate if this research will include any of the following procedures

✓ Collection of Biological Specimens
✓ Medication-Free Period or Treatment Washout

Population

Indicate which of the following populations will be included in this research

✓ Medically and Psychiatrically Healthy Subjects
✓ Adults
✓ Employees or Students

Research Support/Funding

Will an existing internal account be used to support the project?
Yes
Describe internal account

This pilot study will be supported by Division of Behavioral Medicine funding.

Under: Funding Source #1

Is the project externally funded or is external funding planned?
No

Study Location

Indicate if the research is/will be conducted at any of the following
✓ Other Columbia University Medical Center Facilities
This protocol describes research conducted by the PI at other facilities/locations
No

Uploaded Protocol Summary Form

Upload Document

Select file to upload.
Peanuts_PSF_051018_Bolded.pdf

Lay Summary of Proposed Research

Lay Summary of Proposed Research

We will enroll and randomly assign 30 sedentary, healthy overweight men and women to two groups. Participants will either start by consuming peanuts for 4 weeks, and then go on to exercise at high intensity intervals (HIIT) for 4 weeks, or the reverse order. We will test and compare the effect of peanuts and exercise on inflammation and heart rate variability as indicators of heart health. Specifically, we will measure inflammation in the blood because there is evidence that higher inflammation is found in heart disease patients [1, 2]. There is also evidence that inflammation is related to death as a result of heart disease in healthy individuals [3-5]. Finally, there are ongoing trials targeting these markers to improve heart health (Entrace, CIRT, CANTOS[bs3]). We hypothesize that peanuts and exercise will reduce inflammation. We also expect to find less inflammation because exercise and peanut consumption activate a part of the nervous system that has been shown to cause a similar effect.
Additionally, previous studies show that inflammation involves the mitochondria in the cell, the part of the cell that produces energy [57]. For this reason, we expect that exercise and peanuts will cause changes in the mitochondria. We will test and compare mitochondrial activity in response to peanut consumption and exercise.

Description of Subject Population

Sample #1

Specify subject population
Overweight or obese (BMI 27-34.9 kg/m2), but otherwise healthy adults (21-45 years of age)
Number of completers required to accomplish study aims
20
Projected number of subjects who will be enrolled to obtain required number of completers
30
Age range of subject population
21-45

Gender, Racial and Ethnic Breakdown
We will aim to recruit 15 male and 15 female participants in proportions comparable to those in the CUMC community (17% African American, 11% Hispanic, 16% Asian, and 48 % white).
Description of subject population

Overweight or obese (BMI 27-34.9 kg/m2), but otherwise healthy adults (21-45 years of age)

Recruitment Procedures

Describe settings where recruitment will occur
Recruitment will occur through flyers posted in CUMC and NYSPI facilities, the surrounding community, **and the Columbia RecruitMe portal.**
How and by whom will subjects be approached and/or recruited?
Recruitment will occur through flyers posted in CUMC and NYSPI facilities, the surrounding community, **and the Columbia RecruitMe portal.**
How will the study be advertised/publicized?
Recruitment will occur through flyers posted in CUMC and NYSPI facilities, the surrounding community, **and the Columbia RecruitMe portal.**
Do you have ads/recruitment material requiring review at this time?
Yes
Does this study involve a clinical trial?
Yes
Please provide the NCT Registration Number
NCT03212144

Concurrent Research Studies

Will subjects in this study participate in or be recruited from other studies?
No

Waiver of Consent/Authorization

Indicate if you are requesting any of the following consent waivers
Waiver of consent for use of records that include protected health information (a HIPAA waiver of Authorization)
No
Waiver or alteration of consent
Yes
Waiver of documentation of consent
No
Waiver of parental consent
No

Consent Procedures

Is eligibility screening for this study conducted under a different IRB protocol?
No
Describe procedures used to obtain consent during the screening process
After phone screening to determine eligibility, participants will complete the Baecke Physical Activity Questionnaire. Those who are regular exercisers, defined as a score of > 2 on this 5-point scale, will be excluded from further participation.
Describe Study Consent Procedures
Informed consent will be documented with a signed consent statement giving a description of the study in detail. In the Consent Form and through discussion with a research assistant, participants will be advised fully of the study procedures, time required, the possible risks and benefits of participation, their right to refuse participation in the study without prejudice, their right to terminate participation at any moment without prejudice, and the name and telephone number of the Investigators.
Indicate which of the following are employed as a part of screening or main study consent procedures
✓ Consent Form

Justification for Waiver or Alteration of Consent

Waiver of consent is requested for the following
During a phone screen, we will request basic information to determine initial eligibility for the study.
Explain why your research can not be practicably carried out without the waiver or alteration

Determination of eligibility is based on a series of steps, beginning with a brief telephone screen after receiving verbal permission from participants to answer questions about the most basic eligibility matters;

age, height, weight. Those meeting these qualifications will be invited to continue with the study or can be excluded. Those who are eligible to continue will come to the Medical Center for an in-person session and provide informed consent before providing any additional information.

Describe whether and how subjects will be provided with additional pertinent information after participation
Information will not be provided to subjects after participation.

Persons designated to discuss and document consent

Select the names of persons designated to obtain consent/assent
acosta, carlos
Alphonsus, Andrea
Lauriola, Vincenzo
Mahmoodi, Amir
Type in the name(s) not found in the above list

Methods to Protect Confidentiality

Will the study be conducted under a certificate of confidentiality?
No

Compensation and/or Reimbursement

Will compensation or reimbursement for expenses be offered to subjects?
Yes
Please describe and indicate total amount and schedule of payment(s).
Include justification for compensation amounts and indicate if there are bonus payments.

Participants will receive $25 for each blood draw, $25 for each sub-maximal cardiopulmonary exercise test, and $50 if they achieve 85% adherence to both the exercise and dietary arms of the study, totaling at most $250. Payments for the blood draws and exercise tests will be made after each test.

Uploads

Upload copy(ies) of unbolded Consent Form(s)
Peanuts_CF_051018_UnBolded.pdf
Upload copy(ies) of bolded Consent Form(s)
Upload copy(ies) of recruitment materials/ads to be reviewed
Peanuts_Flyer_Unstamped.pdf

Upload copy(ies) of the HIPAA form
Peanuts_HIPPA-Form-A.pdf
Peanuts_HIPPA-NYSPI.pdf
Peanuts_Phone-Screen-Waiver.pdf
Upload any additional documents that may be related to this study

Cover Page

Protocol Number: 7466 Version Date: 5/10/2018

Protocol Title: The Anti-Inflammatory Effects of Exercise and Peanut Consumption

Principal Investigator: Richard P. Sloan, PhD

Email:rps7@columbia.edu

Telephone: 646-774-8940

Office: Cell Phone:

Lay Summary

This section is intended to provide a basic overview of the study including a description of its purpose, methods, and subject population. The summary should provide a concise overview of the study for non-scientific and scientific members of the IRB. Please avoid medical or technical terminology. In general, the abstract of a grant does not provide a suitable lay summary.

Please also paste of a copy of the Lay Summary into the PRISM PSF Form.

We will enroll and randomly assign 30 sedentary, healthy overweight men and women to two groups. Participants will either start by consuming peanuts for 4 weeks, and then go on to exercise at high intensity intervals (HIIT) for 4 weeks, or the reverse order. We will test and compare the effect of peanuts and exercise on inflammation and heart rate variability as indicators of heart health. Specifically, we will measure inflammation in the blood because there is evidence that higher inflammation is found in heart disease patients [1, 2]. There is also evidence that inflammation is related to death as a result of heart disease in healthy individuals [3-5]. Finally, there are ongoing trials targeting these markers to improve heart health (Entrace, CIRT, CANTOS[bs3]). We hypothesize that peanuts and exercise will reduce inflammation. We also expect to find less inflammation because exercise and peanut consumption activate a part of the nervous system that has been shown to cause a similar effect.

Additionally, previous studies show that inflammation involves the mitochondria in the cell, the part of the cell that produces energy [57]. For this reason, we expect that exercise and peanuts will cause changes in the mitochondria. We will test and compare mitochondrial activity in response to peanut consumption and exercise.

Background, Significance, and Rationale

In this section, provide a brief summary of the status quo of the relevant work field, and how the proposed study will advance knowledge. Specifically, identify the gaps in knowledge that your project is intended to fill. If no gaps exist that are obviously and directly related to your project, explain how your proposed research will contribute to the overall understanding of your field. Describe potential impacts of your project within your field of study and in a broader context. Provide a critical evaluation of existing knowledge. The literature review does not have to be exhaustive.

Consensus panels consistently recommend that elements of a healthy lifestyle include consumption of fruits, vegetables, whole grains, nuts, and fish and increased physical activity for prevention of heart disease [6]. Just as consistently, Americans ignore this advice. In 2012, <1% of all US adults met 4 of 5 healthy dietary goals and nearly one third engaged

in no aerobic leisure-time physical activity [7]. Simply put, people find it extremely difficult to achieve these health-promoting dietary and activity goals [8].

Certain lifestyle modifications, e.g., nut consumption and aerobic exercise, appear to exert cardioprotective effects. A substantial body of evidence now demonstrates the beneficial impact of nut consumption on cardiovascular disease outcomes and all-cause mortality. In the Adventist Health Study, participants who consumed nuts 5 or more times per week had significantly reduced risks of both fatal coronary heart disease and nonfatal myocardial infarction [9]. The Iowa Women's Health Study and the PREDIMED trial reported similar findings [10-12]. Nut consumption was associated with a decreased prevalence of risk factors for CVD in 13,292 participants in NHANES [13]. Very recent studies report that nut consumption was inversely associated with total mortality and with deaths due to heart disease, cancer, and respiratory disease in over 115,000 women and men in the Nurses' Health Study and the Health Professionals Follow-up Study [14] and in ethnically diverse cohorts of over 200,000 participants [15].

Observational and intervention studies of nut consumption also have shown reductions in various chronic diseases mediators, including oxidative stress [16, 17], hyperglycemia [13, 18], hyperlipidemia [10, 18], blood pressure [19, 20], cardiovascular autonomic regulation [20], and endothelial dysfunction [11]. Nut consumption may have anti-inflammatory effects [21, 22], a cardioprotective mechanism of particular interest.

Similarly, many studies report that aerobic conditioning enhances vagally mediated high frequency (HF) HRV [23-27] and has anti-inflammatory effects [28-30]. Finally, studies from our group [31, 32] and others [33-37] show modest but consistent inverse relationships between HRV and inflammatory indices, often in large and nationally representative datasets. Thus, evidence suggests the possibility that nut consumption and exercise could result in increases in HRV and reduction of inflammation, outcomes that are associated with cardioprotective effects.

However, this evidence is weaker than generally assumed. There appear to be no studies of the anti-inflammatory effects of peanut consumption. Many studies of the effect of exercise on heart rate [38-40] or HRV [23, 41-43] report no effect or no difference between trained and sedentary participants and many that do show effects are cross-sectional comparisons of highly trained athletes with sedentary controls or longitudinal studies of training that have only a small number of participants [23, 44], lack a control group [45], or include only men [24, 26, 27, 46-49]. Thus, the data on the effect of exercise on inflammation must be regarded as promising but not fully established.

With regards to mitochondria, previous studies reveal that systemic inflammation involves mitochondrial signaling through several routes [57, 58]. A direct pathway by which this occurs is the leaking of mitochondrial circular DNA (mtDNA) in the systemic circulation in response to mitochondrial dysfunction, cellular damage or oxidative stress [57]. MtDNA are recognized as foreign or immunogenic and thereby trigger inflammation [59]. The indirect course involves the release of immunogenic molecules in the cell cytoplasm that induce proinflammatory gene response and the release of cytokines in various cells [59]. Finally, mtDNA encodes and modulates the electron transport chain whereby it ensures the proper detoxification of reactive oxygen species (ROS), and hence mitochondria can carry out its functions to produce energy and regulate major stress-response axes [60]. It follows that mitochondrial dysfunction may be directly associated with various pathologic states [60].

The potential pathophysiology of mitochondrial dysfunction requires a better understanding of the efficacy of various interventions in regulating mitochondrial function. Recent findings contend that vagus nerve activation and the release

of acetylcholine prevents inflammatory stimulation and mtDNA release [58]. Therefore, given the abovementioned studies linking nut consumption to reduced oxidative stress [16,17], and exercise to high vagal activity [27], we endeavor to examine the response of mitochondria to both interventions. Particularly, we will extract peripheral blood mononuclear cells (PBMCs) to examine mtDNA and mitochondrial enzymatic activity.

Finally, with regards to the duration of exposure to both interventions, several studies of the effect of nut consumption on a variety of outcomes including inflammatory and autonomic show effects after 4 weeks. We modeled our intervention on those studies. Similarly, recent studies of high intensity interval training show effects on a variety of outcomes with as little as 2 weeks of training. Most use a 4-week program.

Selecting peanuts over other nuts was a compromise taking into consideration several factors. The best evidence for anti-inflammatory effects of nuts is in interventional studies of pistachio nuts. For example, West et al. [19] and Sauder et al. [20] found lipid lowering, anti-hypertensive, and anti-inflammatory effects of 4 weeks of consumption of pistachio nuts. The best evidence on peanut consumption comes from an observational study by Bao et al. [14] who showed substantial effects on mortality from diets heavy in a variety of nuts including peanuts. Thus, although the evidence of an anti-inflammatory effect of nuts is stronger for pistachios, peanuts are much cheaper and since the overall premise of this study is to test a public health intervention, we decide to test peanuts in this pilot grant.

This application is based on the discrepancy between consensus recommendations and the reality of health behavior change, and is informed by the opportunity to exploit what appears to be a common pathway by which nut consumption and exercise may exert their cardioprotective effects: the cholinergic anti-inflammatory reflex {Tracey, 2002 #6544}. Through this reflex, acetylcholine released by the vagus nerve effectively inhibits cytokine production in the principal organs of the innate immune system, the reticuloendothelial system in the spleen and the liver [50, 51].

Specific Aims and Hypotheses

Concisely state the objectives of the study and the hypothesis or primary research question(s) being examined. There should be one hypothesis for every major study procedure or intervention. For pilot studies, it is important not to overstate the study's objectives. If there are no study hypotheses, describe broad study goals/aims.

Hypothesis/Objectives

We propose to conduct an innovative pilot crossover non-inferiority trial to collect preliminary data with the aim, ultimately, of testing the hypothesis that the anti-inflammatory effect of peanut consumption is at least as great as that of short term (four week) high-intensity aerobic exercise.

Our aims are to test the hypotheses that:

1. Plasma levels of IL-6 and TNF-α are reduced by peanut consumption and that this effect is at least as great as the effect of high-intensity aerobic exercise.

2. Consistent with the cholinergic anti-inflammatory hypothesis, peanut consumption and high intensity exercise will be associated with an increase in heart rate variability.

3. Mitochondrial enzymatic activity is altered in response to both interventions: exercise and peanut consumption

Inclusion/Exclusion Criteria

This section details your study sample(s) and addresses the requirement for risk minimization.
You may choose to divide your sample by population (healthy controls vs. subjects) or by procedure (subjects who will have an MRI) and then define different sets of criteria for each.

For each sample, create or insert a table to describe detailed criteria for study inclusion and exclusion and the method you will use to ascertain each criterion. The method of ascertainment may describe tests, scales and instruments. When relevant, indicate the level of training of the person who will make the assessment (e.g. clinical interview by a psychiatrist).

Inclusion/Exclusion Criteria needs to be numbered and listed in outline form (see Table template below).

INCLUSION CRITERIA	METHOD OF ASCERTAINMENT
Of either sex, age 21–45 years English-speaker	Telephone screen
Overweight or obese	BMI 27.0 – 34.9 kg/m^2
Sedentary	Baecke Physical Activity Questionnaire of <10
Home computer access	Participant disclosure

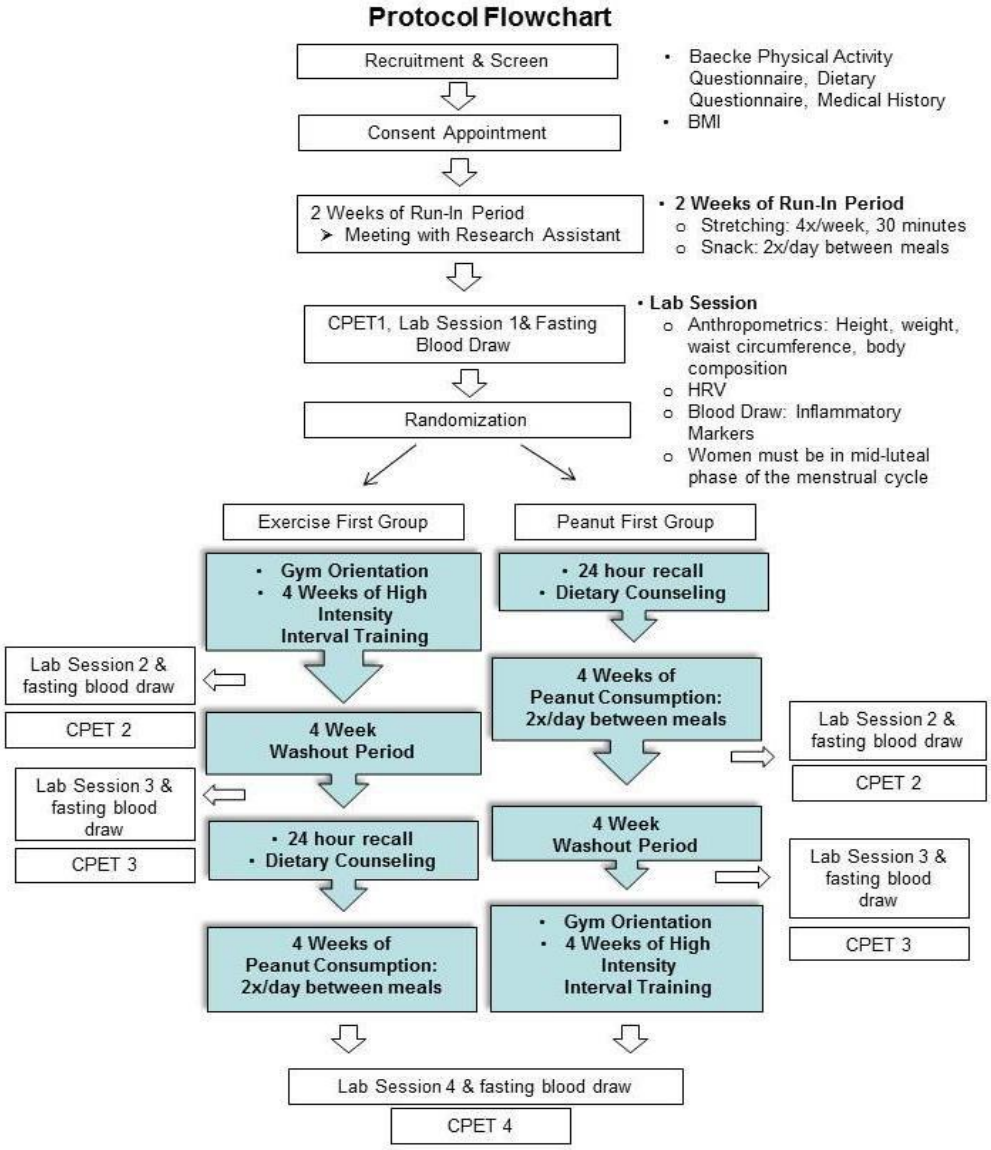
EXCLUSION CRITERIA	METHOD OF ASCERTAINMENT
1. Cardiovascular disease	Medical History Interview
2. Uncontrolled high blood pressure (blood pressure ≥ 140/90). Individuals with controlled hypertension (i.e. under medical treatment) and blood pressure lower than 140/90 will not be excluded.	Measurement taken at consent before eligibility is determined
3. Current or recent (evidence of disease x 5 years) non-skin neoplastic disease or melanoma. Prostatic carcinoma will not be grounds for exclusion.	Medical History Interview
4. Active hepatic disease (not a history of hepatitis) or primary renal disease requiring dialysis, primary untreated endocrine diseases, e.g., Cushing's disease or primary hypothalamic failure or insulin dependent diabetes (Type I or II).	
5. HIV infection	
6. Pregnant or lactating (participation allowed 3 months after ceasing lactation).	
7. Medications that alter inflammation or autonomic nervous system activity.	
8. Any history of psychosis or ECT	

<table>
<tr><td>9. Psychotic disorder (lifetime)</td><td colspan="3" rowspan="2"></td></tr>
<tr><td>10. Current or recent (past 5 years) Major Depressive Disorder, Bipolar Disorder, or Anxiety disorder</td></tr>
<tr><td>11. Current or recent (within past 12 months) alcohol or substance abuse or dependence. Recent use (past month) of recreational drugs.</td><td colspan="3" rowspan="2">Medical History Interview</td></tr>
<tr><td>12. Probiotic and dietary supplements that affect inflammation or the ANS</td></tr>
<tr><td rowspan="5">13. Physically active</td><td>CPET1</td><td>VO_{2max} (ml/kg/min)</td><td>VO_{2max} (ml/kg/min)</td></tr>
<tr><td>Age (yrs)</td><td>Male</td><td>Female</td></tr>
<tr><td>21-29</td><td>>41.0</td><td>>35.2</td></tr>
<tr><td>30-39</td><td>>39.5</td><td>>33.8</td></tr>
<tr><td>40-49</td><td>>37.6</td><td>>32.3</td></tr>
<tr><td>14. Peanut allergy in subject or in family of subject. Subjects who are unsure of their allergy status will be excluded.</td><td colspan="3">Diet Interview</td></tr>
<tr><td>15. Hormonal Birth Control</td><td colspan="3">Telephone Screen</td></tr>
</table>

Study Procedures

Provide a clear, concise narrative of study procedures with special attention to the subjects' involvement. Detail the overall study timeline and location of study procedures, list all interventions, assessments and interviews, estimate the duration of each procedure, provide dosing schedules, identify study personnel involved in each procedure, and provide credentials for relevant personnel. For complicated study designs, we strongly encourage attaching tables, flow-charts, and study algorithms.

Sedentary, overweight or obese but otherwise healthy 21-45 year old participants from Columbia University Medical Center/New York Presbyterian Hospital**,** and surrounding community**,** will be recruited through posted flyers **and the Columbia RecruitMe online platform**. After screening and eligibility determination through physical activity assessment and medical history interview they will provide informed consent. Participants must agree to maintain constant body weight(<±3%) and current levels of physical activity, except for the study interventions, throughout the protocol. They must also agree to abstain from omega-3 fatty acids supplements, high fat fish consumption (>8oz/week), and nuts (besides the peanuts given). Additionally, high quantities (>1 serving/day) of flax seeds, chia seeds, soy, canola, including oils, or food products that contain these ingredients in high quantities must be avoided, but subjects can otherwise maintain their current diet. The experimental protocol is presented in the Flowchart.



Qualifying participants will undergo a two-week run-in period, first of control snack consumption and then stretching to screen for adherence. They will then undergo a submaximal cardiopulmonary exercise test, sCPET 1, to establish baseline VO_{2max} and confirm eligibility as a sedentary individual. They will then proceed to Lab Session 1 .

Women will be asked to wait until they are in the post-ovulatory mid-luteal phase of their menstrual cycle (as indicated by a home ovulation kit) to schedule the first sCPET, such that all their later sCPET and laboratory tests will similarly align with the mid-luteal phase.

Women participants receive a 7-day ovulation home kit at the start of the study to estimate the ovulation date. The kit contains strips on which participants are asked to urinate every day following the end of their menstrual period until ovulation is detected – measured by a surge in luteinizing hormone (LH), also known as the onset of the luteal phase. All study tests are scheduled for this period within the menstrual cycle.

Participants will then be randomized to either 4 weeks of high intensity interval aerobic exercise or peanut consumption (2 times a day). Participants starting with peanuts will meet with the research assistant/dietitian who will assess their eating patterns by implementing a 24 hour recall. Dietary information will be used to help guide the subjects in maintaining an isocaloric diet during the protocol. Additionally, the Miflin St. Jeor calculation will be used to determine the daily number of calories needed for each subject in order to maintain their weight.

All adherent and qualifying subjects go on to Laboratory Session 1 (anthropomorphic indices, HRV, fasting blood drawn). Participants starting with the exercise intervention will be instructed on how to use the exercise facility, and participants starting with peanuts will be given peanuts and instructed on food substitution in order to maintain an isocaloric diet. All contact with participants about group assignment, test scheduling, adherence monitoring, etc. is conducted by trained research assistant "coaches."

After the first 4-week intervention (exercise or peanuts) all participants will undergo Laboratory Session 2 and sCPET 2, and proceed to a 4-week washout period.

By the end of the washout period, all participants will undergo sCPET 3. Participants who cross-over to the dietary peanut intervention will meet with the research assistant/dietitian to assess their eating patterns to inform instructions on maintaining an isocaloric diet during the protocol. Participants who cross-over to the exercise intervention will be instructed on how to use the exercise facility. All participants will return for Laboratory Session, and participants who will be consuming peanuts will be given peanuts and instructed on food substitution in order to maintain an isocaloric diet.

Following the second 4-week intervention, all participants return for follow-up Laboratory Session 4 and sCPET 4. All outcome variables (VO_{2max}, HRV, inflammation, and PBMC's) and control variables (weight, body composition and diet quality and physical activity independent of training) will be collected at 4 time periods in the study. All contact with participants about group assignment, test scheduling, adherence monitoring, etc. is conducted by trained research assistant "coaches."

Two-Week Run-in Period

In previous projects, the run-in period has allowed us to identify participants likely to adhere to the protocol and thus has substantially reduced dropout.

For the first week, participants will eat a run-in snack, commercially available pita chips, twice a day as between meal snacks. Research assistants will collect the numbered pita packets at the end of the week to check for compliance. Only participants who consume at least 11 out of the 14 pita snacks and maintain weight will continue to the second week of the run-in.

For the next week, participants will be instructed on how to perform the stretching phase of the run-in and how to use the Polar Heart Rate (HR) monitor. Participants will complete 4X/week for 30 min of stretching at home while wearing the Polar HR monitor. Coaches will provide detailed instructions on how to complete the stretching.
Stretches consist of arm circles, neck rotations, toe reach, gluteal stretches, lateral leg swings, achilles stretch and ankle rolls. Adherence will be monitored using gym attendance records and HR monitor data. Only participants who perform at least 3 out of the 4 stretching sessions can continue on to the sCPET, Lab Session 1, and randomization.

Submaximal Cardiopulmonary Exercise Test

We will administer a sub-maximal test using a pre-recorded audiotape with instructions and timed metronome rhythms and a 12" step (see figure). The participant will listen to the test instructions and will commence stepping to the metronome beat at 15 steps per minute for a 2-minute period following which heart rate, measured by telemetry (Model RS400, Polar Electro OY, Finland) and rating of perceived exertion on the Borg Scale (see figure) will be recorded (Test Level 1). The step rate then will be increased to 20 steps per minute for an additional 2 minutes, when heart rate and rating of perceived exertion will again be recorded (Test Level 2). The test will continue with additional 2 min increments increasing the step rate by 5 steps/min until the participant reaches a heart rate of 80% of the predicted maximal heart rate equation (220-age) or estimates perceived exertion at a score of 17 or greater. The maximum test duration will be 10 minutes (i.e., Test Level 5). Each individual's aerobic capacity then will be predicted by plotting the exercise heart rates on a prepared graphical datasheet, drawing a visual line of best fit between the data points, projecting the line up to maximum heart rate (HR) and estimating the corresponding aerobic capacity (ml O_2/kg/min) from the x-axis. This estimate of aerobic capacity will be used to establish target heart rate for the 4-week training period. Additionally, as illustrated in inclusion criteria chart, the sCPET1 will be used to determine sedentary status which is a requirement for subjects.

6	No exertion
7	
8	
9	
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	
20	Maximal exertion

Dietary Assessment

Participants who have successfully completed the run-in, the sCPET1, who have been randomized, and who are beginning the peanut intervention will meet with a research assistant who will assess their eating patterns using a 24 hour recall (USDA Multiple-Pass Method [52]). This will inform recommendations for a stable, isocaloric eating pattern. Subjects must refrain from consuming foods or supplements listed in exclusion criteria. Caloric needs are calculated using the Miflin-St Jeor prediction equation [53].

Participants must abstain from omega-3 fatty acids supplements and high fat fish consumption (8oz/week), nuts, flax seeds and chia seeds, soy (including soybean oil and canola oil) and food products that contain these ingredients in high

quantities (>1 serving/day) during the study but can otherwise maintain their current diet. Participants are assessed for alcohol, caffeine, and cocoa consumption and must maintain their levels of intake of throughout the study.

Laboratory Testing Sessions

Participants abstain from any physical exercise for a 24-hour period prior to each testing session to control for acute effects of exercise on inflammatory markers. Participants arrive for Laboratory Sessions in the morning after an overnight fast. 45 ml (9 teaspoons) of venous blood will be drawn for cytokine, PBMCs and hormone analysis. For women, laboratory sessions are scheduled in the mid-luteal phase of the menstrual cycle, to control for cycle effects on Heart Rate Variability [54]. After the blood draw, they receive a light breakfast providing 15% daily energy intake as established during the dietary assessment. Waist circumference is measured with a Gulick anthropometric tape. Height is measured using the Seca 214 Portable Height Rod (Seca Corp., Hamburg, Germany). Weight and body composition are measured using a Tanita BF-350 monitor (Tanita UK Ltd., Middlesex, UK).

Participants then are instrumented with ECG leads and respiration monitoring bands and rest quietly in the supine position for 5 min, after which 20 min of resting ECG and respiration data are collected. These data are collected in all Laboratory Sessions.

Treatment Conditions

In this crossover design, participants are randomly assigned to either the peanut condition followed by aerobic exercise or aerobic exercise followed by the peanut condition. Following the guidelines for non-inferiority trials, the exercise intervention, as the more widely accepted anti-inflammatory treatment, functions as the comparison for the peanut intervention.

Peanut Diet

Regular daily caloric intake of each subject will be estimated using data from 24hr recalls, the Miflin-St. Jeor equation, and stress/activity factors. Participants will consume dry roasted, unsalted peanuts equivalent to approximately 10% of daily energy intake twice a day (total=20% total daily energy intake), which will range from approximately 400kcal to 600 kcal, which corresponds to about 2.4 ounces to 3.6 ounces. Peanuts will replace protein and fat containing foods so that the daily caloric intake will not differ from participants' typical diet. Nutrient content will be analyzed by Covance Laboratory (Madison WI). To assess compliance, participants will be asked to bring back the empty, numbered peanut packets by the end of every week and will be given new packets weekly. Additionally, subjects will be informed that they will be randomly assessed weekly for compliance; they will be asked to provide details of when and where they consumed their packets the previous day. Research assistants will provide guidance on how to maintain compliance.

High Intensity Interval Training (HIIT):

Based on previous studies [55], participants will engage in 4 training sessions per week over a 4-week period, with 24 hour rest-periods between each training day. Participants will have the option to exercise either at the PlusOne Fitness Center at CUMC/NYPH, or at home on a Sunny Folding Climbing Stepper (Sunny Health & Fitness, Los Angeles) which will be delivered to the participant via UPS or FedEx, and be retrieved by Behavioral Medicine staff at the end of the study,

at no cost to them. Participants will indicate which exercise modality they choose at the informed consent appointment, and those who elect to do the home-based program will have the Sunny Stepper delivered to their home after the 2-week run-in period is completed. Each session begins with a 3 min low intensity warm-up, and then participants exercise as rapidly as they can for 20 seconds, aiming to reach 85% of their maximum heart rate as established during the submaximal cardiopulmonary exercise testing (sCPET) (see Sec D.3.4.). This 20 second period is followed by 40 seconds of low intensity exercise. Participants complete 8 such intervals for sessions 1 and 2, 10 intervals for sessions 3 and 4, and 12 intervals thereafter. A brief training program similar to this yielded a 9% increase in VO_2max in only 12 days. High Intensity Interval Training (HIIT) also has been shown to be safe. In over 175,000 hours of cardiac rehabilitation, the cardiovascular event rate was extremely low [56].

Criteria for Early Discontinuation

Define criteria that will be used to exit or drop subjects from the study. Indicate the time points when such criteria will be applied, and describe the rating instruments, parameters, and thresholds that will lead to a decision to terminate a subject's participation. In addition, explain procedures for managing subjects who are dropped from the protocol.

For treatment studies: To minimize risks to subjects, operationalized drop-out criteria should be defined so that subjects who worsen, or in some cases, fail to improve, are removed from the study and offered standard care. The threshold for drop-out should consider the level of risk associated with non-improvement for the specific disorder, the availability of alternatives, and the typical required duration of treatment. For example, emergence of suicidal intent, or psychosis, should prompt immediate clinical evaluation and withdrawal from the study.

Subjects will be dropped from the study at any point during the entire study in the event of serious illness or injury, or if they develop an allergy to peanuts or at any point during the exercise phase if an injury occurs. All participants will have been carefully screened prior to the initiation of the exercise protocol to minimize the risk of adverse events. Participants will be required to present a note from a physician indicating medical clearance for exercise training.

Blood and other Biological Samples

Describe how the sample will be used and indicate, when relevant, the amount of the sample. The IRB wants to know that the sample is sufficient for the purposes of the study, but that sampling is limited to what is minimally necessary.

If you've indicated that you intend to store a sample for future use, indicate where the sample will be stored, how long the sample will be stored, and to what purposes the sample will eventually be put. Check the IRB website at http://irb.nyspi.org/irbdnn/Policies/GeneticResearch/tabid/96/Default.aspx for specific guidance and additional information about future use of DNA samples.

Assay	mL	Purpose
blood	45 ml	Cytokine (plasma), neuroendocrine factors (plasma), and peripheral blood mononuclear cells isolation (PBMCs)

Assessment Instruments

List all assessment instruments, indicate who will administer them, and provide an estimate the duration of each. The IRB wants to know that assessments instruments are appropriate measures for the purposes of the study and are no more burdensome than is necessary. The IRB will consider the burden of assessment instruments (in terms of time, sensitivity of material, etc.) in the risk/benefit analysis. Please attach copies or otherwise provide all non-standard instruments.

Instrument	Variables Measured
Baecke Physical Activity Questionnaire	Initial assessment of sedentary status
Polar Heart Rate monitor*	heart rate during exercise training and protocol adherence
Miflin-St Jeor prediction equation	Estimate resting metabolic caloric needs
Gulick anthropometric tape	Waist circumference
Seca 214 Portable Height Rod (Seca Corp., Hamburg, Germany).	Height
Tanita BF-350 monitor (Tanita UK Ltd., Middlesex, UK).	Weight and body composition
24 hr recall USDA Multiple-Pass Method	Daily diet
ECG	Heart rate variability
Clearblue Fertility Monitor Test Sticks	Ovulation Date

*Throughout all training sessions, patients will wear polar heart rate monitors that record HR throughout the session. These data will be uploaded to a secure Polar cloud-based server and evaluated after each session. This will assist in adherence and will provide rigorous documentation of training intensity levels. Anonymous Gmail email accounts will be set up for each participant with the help of their RA coach to make sure they do not include any identifying information, and these accounts will be tied to the Polar heart rate devices. Heart rate data for exercise session will be stored in the cloud identified only by this anonymous email account, which will only be used for the study for logging Polar data. Polar data is uploaded through either at-home wifi or via a cable link to a laptop and desktop computer. Subjects will be instructed to use these two methods to prevent association of their mobile phone number with their heart rate data in the cloud.

Research Related Delay to Treatment

Research involving participants who are in need of treatment invariably involves delay to care, and this delay is associated with risk. Scheduling of procedures must be carefully organized to minimize delay. Other delay must involve only that minimally necessary to accomplish the aims of the research while respecting subject well- being and safety. Describe the delay, by virtue of research participation in this study, before a participant can receive treatment of known efficacy or standard care routinely offered in the community.

This is not a treatment study, so there is no delay to treatment that participants may need to receive.

Clinical Treatment Alternatives

Describe what other treatment or assessment options are available to subjects who do not participate in research.

This is not a treatment study, so the alternative to participation is not to participate.

Risks/Discomforts/Inconveniences

"Risk" is a broad term used to convey the potential for harm, burden, and inconvenience related to research participation. Use this section to provide a comprehensive description of foreseeable physical, psychological, social, interpersonal, and economic risks introduced by the research. Include the source of the information. Consider both the probability and magnitude of harm and its impact. Describe the foreseeable harms associated with the research (untoward effects of a medication) and those related to delay to individualized treatment. Include data from the literature, and local data, if available, on risk rates and subject experiences with research procedures. Describe

procedures in place to minimize risk. In general, please create a numbered list of risks/categories of risk, and in general put the list in the order of significance or level of risk, the most significant risks first followed by others.

1.Submaximal Cardiopulmonary Test Risks

There exists the possibility of certain changes occurring during the test. These include abnormal blood pressure; fainting; irregular, fast, or slow heart rhythm; and, in rare instances, heart attack, stroke, or death. Every effort will be made to minimize these risks by evaluation of preliminary information relating to the participant's health and fitness and by careful observation during testing. Emergency equipment and trained personnel are available to deal with unusual situations that may arise. Since this is a submaximal exercise test, the risks associated are those typical of any physical activity, and are low.

The submaximal cardiopulmonary exercise test will conducted in the Behavioral Medicine laboratory on the 16th floor of the Presbyterian Hospital Building. It will be administered by Vincenzo Lauriola, a Masters level exercise physiologist. According to the Handbook of Sports Medicine and the American College of Sports Medicine [6], participants at low risk can be supervised during this test by non-physicians without a physician being immediately available. Mr. Lauriola is certified at a level of basic life support (cardiopulmonary resuscitation [CPR]) and has automated external defibrillator (AED) training. The exercise testing facility also has a written medical emergency response plan with procedures and contact numbers and is equipped with an AED.

2.Training Program Risks

The risks associated with exercise training are those typical of any physical activity. All participants will have been carefully screened prior to the initiation of the exercise protocol to minimize the risk of adverse events.

Participants will be required to present a note from a physician indicating medical clearance for exercise training.

3.Blood Draw Risks

Blood samples will be drawn by trained phlebotomists.

During the blood draw, the participant may feel slight pain from the needle or experience some dizziness. She may also develop a temporary bruise where the needle was inserted.

4.Peanut Consumption Risks

Although we are currently unaware of any risks, there may be possible risks to the dietary intervention, such as previously unknown allergies.

Subjects will be screened for known peanut allergies and monitored for signs of allergic reactions.

Methods to Protect Confidentiality

Describe the data management plan and the methods you will employ to protect subject privacy and the confidentiality of research data. The section should detail how information will be collected, recorded, coded, stored, transmitted, and as applicable, shared with other investigators so as to minimize risks related to breach of confidentiality. Confirm that

identifiers are removed, to the extent possible, from research data, and explain if there are links between subject identity and research data, or if the data is anonymous. Also, indicate where the data is stored, who is responsible for its safekeeping, and who has access to subject identity and codes, if any, which cross-link research data and subject identity. Confirm that identifiable data is not collected, stored, or transmitted by mail, fax, on removable drives, laptops, or via the internet without proper protections, e.g. encryption.

There are two areas in which safeguards to protect participants from undue risk require discussion: procedures used to obtain informed consent and those used to insure confidentiality of participants' responses and findings on tests. In the consent form and in discussion with an investigator, participants will be advised fully of the procedures to be used, the amount of time required of them, the possible risks and benefits of the procedures, their right to refuse participation in the study without prejudice, their right to terminate participation at any moment without prejudice, and the name and telephone number of the Principal Investigator. In the informed consent form, participants are told that the information they provide and all findings will be kept strictly confidential, with access limited to the research staff and the possible exception of state or federal regulatory personnel. No one but designated project staff will have access to the master list linking participants' names to subject identification numbers, and all information obtained will be coded. Data will be analyzed without reference to personal identifying information, and this information will be carefully protected within the database. All paper files will be kept in locked file cabinets.

Direct Benefits to Subjects

Describe only benefits to individual subjects that are likely to accrue during the study itself. Do not include subject compensation or treatment to be provided at the end of the study, as these do not figure into the IRB's risk benefit considerations. Do not describe diagnostic and evaluation components unless subjects receive clinical feedback. Do not describe the anticipated scientific benefits of the research. Some studies offer no direct benefit to subjects.

The cardiorespiratory benefits of moderate exercise are well known. Additionally, evidence suggests that peanut consumption is also cardioprotective; a substantial body of evidence exists that demonstrates the beneficial impact of nut consumption on cardiovascular disease outcomes and all-cause mortality. Any information that is important to the participant's health will, with the participant's written permission, be transmitted to their physician.

References

1. Ridker, P.M. and T.F. Luscher, *Anti-inflammatory therapies for cardiovascular disease.* Eur Heart J, 2014. **35**(27): p. 1782-91.
2. Sarwar, N., et al., *Interleukin-6 receptor pathways in coronary heart disease: a collaborative meta-analysis of 82 studies.* Lancet, 2012. **379**(9822): p. 1205-13.
3. Ridker, P.M., et al., *Plasma Concentration of Interleukin-6 and the Risk of Future Myocardial Infarction Among Apparently Healthy Men.* Circulation, 2000. **101**(15): p. 1767-1772.
4. Ridker, P.M., et al., *C-Reactive Protein and Other Markers of Inflammation in the Prediction of Cardiovascular Disease in Women.* New England Journal of Medicine, 2000. **342**(12): p. 836-843.
5. Schnabel, R.B., et al., *Multiple Inflammatory Biomarkers in Relation to Cardiovascular Events and Mortality in the Community.* Arteriosclerosis, Thrombosis, and Vascular Biology, 2013. **33**(7): p. 1728-1733.
6. Pearson, T.A., et al., *American Heart Association Guide for Improving Cardiovascular Health at the Community Level, 2013 Update: A Scientific Statement for Public Health Practitioners, Healthcare Providers, and Health Policy Makers.* Circulation, 2013. **127**(16): p. 1730-1753.
7. Go, A.S., et al., *Executive Summary: Heart Disease and Stroke Statistics—2014 Update: A Report From the American Heart Association.* Circulation, 2014. **129**(3): p. 399-410.
8. Ebrahim, S., et al., *Multiple risk factor interventions for primary prevention of coronary heart disease.* Cochrane Database Syst Rev, 2011(1): p. CD001561.
9. Fraser, G.E., et al., *A possible protective effect of nut consumption on risk of coronary heart disease. The Adventist Health Study.* Arch Intern Med, 1992. **152**(7): p. 1416-24.
10. Sabate, J., et al., *Effects of walnuts on serum lipid levels and blood pressure in normal men.* N Engl J Med, 1993. **328**(9): p. 603-7.
11. Ma, Y., et al., *Effects of walnut consumption on endothelial function in type 2 diabetic participants: a randomized controlled crossover trial.* Diabetes Care, 2010. **33**(2): p. 227-32.
12. Guasch-Ferre, M., et al., *Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial.* BMC Med, 2013. **11**: p. 164.
13. O'Neil, C.E., et al., *Nut consumption is associated with decreased health risk factors for cardiovascular disease and metabolic syndrome in U.S. adults: NHANES 1999-2004.* J Am Coll Nutr, 2011. **30**(6): p. 502-10.
14. Bao, Y., et al., *Association of Nut Consumption with Total and Cause-Specific Mortality.* New England Journal of Medicine, 2013. **369**(21): p. 2001-2011.
15. Luu, H.N., et al., *Prospective evaluation of the association of nut/peanut consumption with total and cause-specific mortality.* JAMA Internal Medicine, 2015.
16. Torabian, S., et al., *Acute effect of nut consumption on plasma total polyphenols, antioxidant capacity and lipid peroxidation.* J Hum Nutr Diet, 2009. **22**(1): p. 64-71.
17. Jenkins, D.J.A., et al., *Almonds Decrease Postprandial Glycemia, Insulinemia, and Oxidative Damage in Healthy Individuals.* The Journal of Nutrition, 2006. **136**(12): p. 2987-2992.
18. Jenkins, D.J., et al., *Nuts as a replacement for carbohydrates in the diabetic diet.* Diabetes Care, 2011. **34**(8): p. 1706-11.
19. West, S.G., et al., *Diets containing pistachios reduce systolic blood pressure and peripheral vascular responses to stress in adults with dyslipidemia.* Hypertension, 2012. **60**(1): p. 58-63.
20. Sauder, K.A., et al., *Pistachio Nut Consumption Modifies Systemic Hemodynamics, Increases Heart Rate Variability, and Reduces Ambulatory Blood Pressure in Well-Controlled Type 2 Diabetes: a Randomized Trial.* Journal of the American Heart Association, 2014. **3**(4).
21. Kiecolt-Glaser, J.K., *Stress, food, and inflammation: psychoneuroimmunology and nutrition at the cutting edge.* Psychosom Med, 2010. **72**(4): p. 365-9.
22. Salas-Salvado, J., et al., *The effect of nuts on inflammation.* Asia Pac J Clin Nutr, 2008. **17 Suppl 1**: p. 333-6.

23. De Meersman, R.E., *Respiratory sinus arrhythmia alteration following training in endurance athletes.* European Journal of Applied Physiology, 1992. **64**: p. 434-436.
24. Yamamoto, K., et al., *Effects of endurance training on resting and post-exercise cardiac autonomic control.* Med Sci Sports Exerc, 2001. **33**(9): p. 1496-502.
25. Seals, D.R. and P.B. Chase, *Influence of physical training on heart rate variability and baroreflex circulatory control.* J Appl Physiol, 1989. **66**(4): p. 1886-95.
26. Tulppo, M.P., et al., *Effects of aerobic training on heart rate dynamics in sedentary participants.* J Appl Physiol, 2003. **95**(1): p. 364-372.
27. Hautala, A.J., et al., *Cardiovascular autonomic function correlates with the response to aerobic training in healthy sedentary participants.* Am J Physiol Heart Circ Physiol, 2003. **285**(4): p. H1747-52.
28. King, D.E., et al., *Inflammatory markers and exercise: differences related to exercise type.* Med Sci Sports Exerc, 2003. **35**(4): p. 575-81.
29. Ford, E.S., *Does exercise reduce inflammation? Physical activity and C-reactive protein among U.S. adults.* Epidemiology, 2002. **13**(5): p. 561-8.
30. Rauramaa, R., et al., *Effects of aerobic physical exercise on inflammation and atherosclerosis in men: the DNASCO Study: a six-year randomized, controlled trial.* Ann Intern Med, 2004. **140**(12): p. 1007-14.
31. Cooper, T.M., et al., *Heart rate variability predicts levels of inflammatory markers: Evidence for the vagal anti-inflammatory pathway.* Brain, Behavior, and Immunity, 2015. **49**: p. 94-100.
32. Sloan, R.P., et al., *RR interval variability is inversely related to inflammatory markers: the CARDIA study.* Mol Med, 2007. **13**(3-4): p. 178-84.
33. Marsland, A.L., et al., *Stimulated production of proinflammatory cytokines covaries inversely with heart rate variability.* Psychosom Med, 2007. **69**(8): p. 709-16.
34. Stein, P.K., et al., *Higher levels of inflammation factors and greater insulin resistance are independently associated with higher heart rate and lower heart rate variability in normoglycemic older individuals: the Cardiovascular Health Study.* J Am Geriatr Soc, 2008. **56**(2): p. 315-21.
35. Lampert, R., et al., *Decreased heart rate variability is associated with higher levels of inflammation in middle-aged men.* American Heart Journal, 2008. **156**(4): p. 759.e1-759.e7.
36. von Känel, R., et al., *Relationship between heart rate variability, interleukin-6, and soluble tissue factor in healthy participants.* Brain, Behavior, and Immunity, 2008. **22**(4): p. 461-468.
37. Thayer, J.F. and J.E. Fischer, *Heart rate variability, overnight urinary norepinephrine and C-reactive protein: evidence for the cholinergic anti-inflammatory pathway in healthy human adults.* Journal of Internal Medicine, 2009. **265**(4): p. 439-447.
38. Madden, K.M., W.C. Levy, and J.K. Stratton, *Exercise training and heart rate variability in older adult female participants.* Clin Invest Med, 2006. **29**(1): p. 20-8.
39. Pigozzi, F., et al., *Effects of aerobic exercise training on 24 hr profile of heart rate variability in female athletes.* Journal of Sports Medicine and Physical Fitness, 2001. **41**: p. 101-107.
40. Ueno, L.M. and T. Moritani, *Effects of long-term exercise training on cardiac autonomic nervous activities and baroreflex sensitivity.* Eur J Appl Physiol, 2003. **89**(2): p. 109-14.
41. Boutcher, S.H. and P. Stein, *Association between heart rate variability and training response in sedentary middle-aged men.* European Journal of Applied Physiology, 1995. **70**: p. 75-80.
42. Loimaala, A., et al., *Controlled 5-mo aerobic training improves heart rate but not heart rate variability or baroreflex sensitivity.* J Appl Physiol, 2000. **89**(5): p. 1825-1829.
43. Sacknoff, D.M., et al., *Effect of athletic training on heart rate variability.* American Heart Journal, 1994. **127**: p. 1275-1278.
44. Xia, R., et al., *Influence of recognition errors of computerised analysis of 24-hour electrocardiograms on the measurement of spectral components of heart rate variability.* International Journal of Biomedical Computing, 1993. **32**: p. 223-235.
45. Wilmore, J.H., et al., *Heart rate and blood pressure changes with endurance training: the HERITAGE Family Study.* Med Sci Sports Exerc, 2001. **33**(1): p. 107-16.

46. Bonaduce, D., et al., *Intensive training and cardiac autonomic control in high level athletes.* Med Sci Sports Exerc, 1998. **30**(5): p. 691-6.
47. Sedgwick, A.W., et al., *The effects of physical training on the day and night long-term heart-rates of middle-aged men.* Eur J Appl Physiol Occup Physiol, 1974. **33**(4): p. 307-14.
48. Wyss, C.A., et al., *Cellular actors, Toll-like receptors, and local cytokine profile in acute coronary syndromes.* European Heart Journal, 2010. **31**(12): p. 1457-1469.
49. Shin, K., et al., *Assessment of training-induced autonomic adaptations in athletes with spectral analysis of cardiovascular variability signals.* Japanese Journal of Physiology, 1995. **45**: p. 1053-1069.
50. Bernik, T.R., et al., *Cholinergic antiinflammatory pathway inhibition of tumor necrosis factor during ischemia reperfusion.* J Vasc Surg, 2002. **36**(6): p. 1231-6.
51. Goldstein, R.S., et al., *Cholinergic anti-inflammatory pathway activity and High Mobility Group Box-1 (HMGB1) serum levels in patients with rheumatoid arthritis.* Mol Med, 2007. **13**(3-4): p. 210-5.
52. Moshfegh, A.J., et al., *The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes.* Am J Clin Nutr, 2008. **88**(2): p. 324-32.
53. Mifflin, M.D., et al., *A new predictive equation for resting energy expenditure in healthy individuals.* The American Journal of Clinical Nutrition, 1990. **51**(2): p. 241-7.
54. McKinley, P.S., et al., *The impact of menstrual cycle phase on cardiac autonomic regulation.* Psychophysiology, 2009. **46**(4): p. 904-11.
55. Esfandiari, S., Z. Sasson, and J. Goodman, *Short-term high-intensity interval and continuous moderate-intensity training improve maximal aerobic power and diastolic filling during exercise.* European Journal of Applied Physiology, 2014. **114**(2): p. 331-343.
56. Rognmo, O., et al., *Cardiovascular risk of high- versus moderate-intensity aerobic exercise in coronary heart disease patients.* Circulation, 2012. **126**(12): p. 1436-40.
57 Picard M., Wallace D. C., Burelle Y. *The rise of mitochondria in medicine.* Mitochondrion, 2016. **30**: p. 105–116.
58 Lu, B., Kwan, K., Levine, Y.A., Olofsson, P.S., Yang, H., Li, J., Joshi, S., Wang, H., Andersson, U., Chavan, S.S., Tracey, K.J. *Alpha 7 nicotinic acetylcholine receptor signaling inhibits inflammasome activation by preventing mitochondrial DNA release*. Mol Med, 2014. **14**(20): p. 350-358.
59. Picard, M., Juster, R., Mcewen, B., *Mitochondria Nexus to Allostatic Load Markers*. Psychosomatic Medicine, 2016.
60 Picard M., McManus MJ., Gray JD., Nasca, C., Moffat C., Kopinski, PK., Seifert, EL., McEwen BS., Wallace, DC. *Mitochondrial functions modulate neuroendocrine, metabolic, inflammatory, and transcriptional responses to acute psychological stress.* Proceedings of the National Academy of Sciences of the United States of America, 2015. **112**(48): p. 6614-6623.

COLUMBIA UNIVERSITY
MEDICAL CENTER

Participate in a Peanut and Exercise Research Study!

Are you age 21-45?

OVERWEIGHT but otherwise HEALTHY?

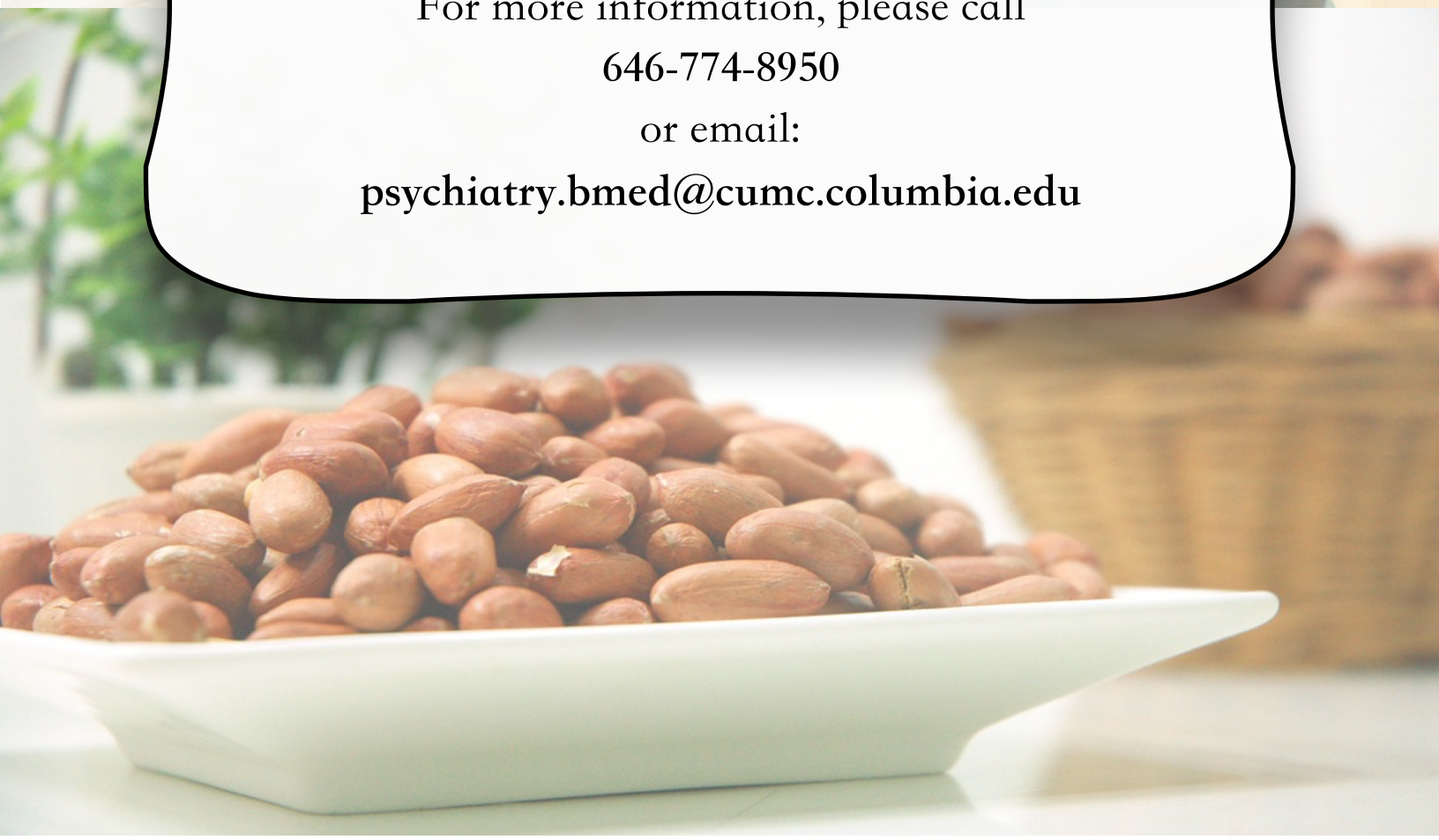
You could earn up to $250 for completing the 14 week study!

For more information, please call

646-774-8950

or email:

psychiatry.bmed@cumc.columbia.edu



Research Subject's Consent Form Cover Sheet
Randomized Crossover Pilot Study: Exercise and Peanut Consumption
PI IRB#: 7466

Overview

Below is a summary of the study in which you are asked to participate. This outline is meant to be a guide for you to use while considering the study and reading the consent form. It is not meant to replace the consent form, which you will have to sign if you decide to participate in the study. The consent form contains detailed information about the study and about the risks which you will need to consider before making your decision. Read the consent form carefully and discuss it with others before deciding to take part. And remember that, even if you agree to participate, you can change your mind at any time.

Purpose of Study

The purpose of this study is to compare the effects of exercise and eating peanuts on inflammation and heart rate variability.

Participation is Voluntary

As with all research, this is a voluntary study, and you do not have to participate if you do not want to. You may stop participating at any time.

Procedures

- **Screening and Eligibility:** You will be asked questions about your health and eating habits over the phone or in person to see if you will be able to take part in the study.

- **Consent Appointment:** You will be asked to read and sign the informed consent form as well as complete some forms and evaluations. If you would like to participate in the study, you will be asked to agree to keep a constant body weight (<±3%), not change your eating habits except for what is asked of you, and keep current levels of physical activity, except for the study interventions, throughout the study. You will also need to present a note from a physician indicating medical clearance for exercise training.

- **Exercise and Diet Trial Period/Run-in**: You will meet with research staff who will guide you in completing a two-week trial period. You will be asked to eat pita chip snacks twice per day for a week, and then for the second week, you will be asked to stretch four times a week for 30 minutes at the gym while wearing a heart rate monitor.

- **Baseline Exercise Test**: If you follow the instructions during the trial period, you will be scheduled to take a baseline exercise test to determine your fitness level.

- **Laboratory Testing Sessions:** Four times throughout the study, you will be scheduled to have your blood drawn and body metrics measured such as height, weight, body composition, and waist circumference. Resting heart rate and other data will also be collected.

- **Dietary Assessment**: You will meet with research staff to complete a dietary assessment in which you will be asked questions about the foods you typically eat.

- **Peanut Intake/Exercise:** You will be randomly assigned to one of two groups. In the peanut group, you will be asked to eat about a handful of roasted, unsalted peanuts twice a day for 4 weeks. In the exercise group, you will be trained and asked to do high intensity interval training four times a week for four weeks. After the four weeks of either eating peanuts or exercising, you will be asked to stop eating peanuts or exercising for 4 weeks. Then you will switch groups to the peanut group if you were in the exercise group or to the exercise group if you were in the peanut group.

Risks

This study includes some risks and discomforts (please refer to the consent form for further details and explanations of these risks). The risks associated with exercise training are those typical of any physical activity. Other risks and discomfort include: discomfort during blood drawing and during the baseline exercise test. Every effort will be made to minimize these risks by evaluation of background information relating to the participant's health and fitness and by careful observations during testing. Emergency equipment and trained personnel are available to deal with unusual situations that may arise.

Benefits

This study is not designed for your direct benefit.

The benefits of moderate exercise are well known. Any information that is important to the participant's health will, with the participant's permission, be transmitted to their physician. Additionally, eating peanuts regularly may reduce the risk of heart disease.

You may contact the Principal Investigator, Richard Sloan at 646-774-8940 with any questions.

Please read and sign the attached consent form for a full description of the study.

Research Subject's Consent Form
Informed Consent for Participation in Research
The Anti-Inflammatory Effects Exercise and Peanut Consumption
PI IRB #7466

Purpose of Study
The purpose of this study is to examine and compare the effects of peanut consumption and aerobic exercise on heart health. You are being asked to participate because you are an overweight and sedentary, but otherwise healthy individual between the age of 21 and 45 years old.

Voluntary
Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any benefits to which you are otherwise entitled. A decision not to participate or withdraw your participation will not affect your current or future treatment at the New York State Psychiatric Institute or Columbia University.

Alternatives to Participation
This is not a treatment study. Information being collected is for research purposes only and is to learn more about the effects of dietary intervention and exercise on cardiovascular health, not about you. The alternative to participating is this study is not to participate.

Procedures
Eligibility During the Study
Your eligibility is checked at multiple times during the early stages of the study through a series of evaluations, questionnaires, and tests done during study meetings. These include a Baecke Physical Activity Questionnaire, Dietary Questionnaire, questions about medical history, and submaximal cardiopulmonary tests. These help to determine whether or not you are able to continue. Also, in the event that you are unable to follow the procedures required, you may be withdrawn from the study.

Consent Session
If you agree to participate you will be asked to meet for less than an hour at the Division of Behavioral Medicine, Department of Psychiatry, on the 15th floor of the Columbia University Medical Center to read and sign the informed consent form and complete additional forms that will be needed for study protocol. You are required to present a note from a physician indicating medical clearance for high intensity aerobic exercise training. Your BMI will be estimated at this time. At this time, you must agree to maintain constant body weight ($\leq \pm 3\%$) and current levels of physical activity, except for the study interventions, throughout the protocol. If you meet the required eligibility criteria, study staff will schedule you for the next appointment.

Two Week Run-in

You will then begin a two-week trial period, or run-in. You will meet at the Division of Behavioral Medicine to receive labeled pita chip snacks and will be asked to eat the snacks twice a day for one week. After one week, you will meet with the research assistant who will collect your labeled packets, determine if you did well enough to continue and provide instructions on how to proceed with the second phase of the run-in. You will be asked to engage in 30 minutes of stretching at home while wearing the Polar Heart Rate (HR) monitor, four times in 1 week. Coaches will provide you detailed instructions on how to perform the stretching and how to utilize the heart rate monitor. After each stretching session, you will upload the data from the heart rate monitor to a secure cloud-based server provided by Polar using an account that is anonymous and does not have any identifiable information contained within. Stretches will consist of arm circles, neck rotations, toe reach, gluteal stretches, lateral leg swings, Achilles stretch and ankle rolls. Your participation will be checked by gym attendance records and HR monitor data. If you sufficiently follow the instructions, you will be able to continue to the next part of the study.

Baseline Exercise Test (CPET)

At the Division of Behavioral Medicine, you will be guided to complete a cardiopulmonary exercise test which takes about 10 minutes. You will be asked to listen to an audiotape test instructions and commence stepping to the metronome beat at 15 steps per minute for a 2-minute period. The step rate then will be increased to 20 steps per minute for an additional 2 minutes. The test will continue to increase in speed until your heart rate reaches 80% of your maximal heart. The maximum test duration will be 10 minutes.

Laboratory Session 1

During the first lab session, your blood will be drawn and your height, weight, and body composition will be measured. Your heart rate will also be measured. You will be asked to wear ECG leads and respiration monitoring bands and rest quietly for 5 minutes, after which 20 minutes of resting ECG and respiration data will be collected. After the blood draw, you will receive a light breakfast. Lab sessions will take about 1 hour and will be conducted at the facilities belonging to the Division of Behavioral Medicine on the 15th and 16th floors of the Columbia University Medical Center.

Dietary Assessment

For about 30 minutes, you will meet with the research assistant at the Division of Behavioral Medicine to assess your eating patterns. You will be guided in how to eat the peanuts without changing your diet too much. You must agree to avoid omega 3 supplements and nuts, and not eat excessive amounts of high fat fish like salmon (>8oz), flax seeds and chia seeds, soy (including soybean oil and canola oil) and food products that contain these (limit to <1 serving a day). You can otherwise maintain your regular diet. You will be asked questions about alcohol, caffeine, and cocoa consumption.

4 Week Period: Peanut Diet

You will be provided with labelled packets of peanuts weekly for four weeks and asked to eat two packets each day and record when and where you consume the peanuts. After each week you will return the empty packets and receive new ones for the next week from the research assistant.

At any point in time during the 4 weeks, a research assistant may ask for details about when and where you ate the peanuts in the last 24 hours.

4 Week Period: Exercise

For four weeks, you will be asked to participate in 4 training sessions per week that last about 20-30 minutes, with 24 hours of rest after each training day. Exercise sessions will take place either at the PlusOne Fitness Center at CUMC/NYPH, or at home on a Sunny Folding Climbing Stepper (Sunny Health & Fitness, Los Angeles) which will be delivered to you via UPS or FedEx, and retrieved by Behavioral Medicine staff at the end of the study, at no cost to. You are free to choose which method you wish to engage in, and will be asked to indicate your choice on this consent document. Each exercise session begins with a 3-minute low intensity warm-up, and then you will exercise aerobically as rapidly as you can for 20 seconds, aiming to reach 85% of your maximum heart rate. This 20 second period is followed by 40 seconds of low intensity exercise. You will be asked to complete 8 such intervals for sessions 1 and 2, 10 intervals for sessions 3 and 4, and 12 intervals for the remaining sessions. Research assistants will provide thorough training for you on how to perform the exercise and how to utilize the heart rate monitor. After each exercise session, you will upload the data from the heart rate monitor to a secure cloud-based server provided by Polar using an account that is anonymous and does not have any identifiable information contained within. Research assistants will be available throughout the week to answer questions about the protocol.

4-week Washout Period:

At the conclusion of the first 4-week period, you will be asked to resume your diet and activity as it was before the intervention. This means that you will be asked to discontinue eating peanuts or discontinue exercising for 4 weeks before continuing on to the second intervention, which will be peanut consumption if you were originally assigned to the exercise group, or exercise if you were originally assigned to the peanut group.

Further Lab Sessions and CPETs

After each 4-week period, including the washout period, you will be asked to complete a set of laboratory sessions in which your fasting blood will be drawn and a cardiopulmonary test like the first one will be given. Lab sessions will take about 1 hour and the cardiopulmonary tests will last at most 10 minutes. Both will be conducted at the same locations as were used previously.

For women only: You will be asked to track and report your menstrual cycle once you enroll in the study. It is very important that we know when you ovulate during the month that you do your first exercise and laboratory. Therefore, we will give you a 7-day ovulation kit at the start of the study, and we will ask you to use this kit so that we can estimate your ovulation date. The ovulation test is a very quick and simple urine test that you will do at home. If for some reason you do not ovulate during this time, we may reschedule your lab and exercise test to the following month, and ask you to monitor your ovulation during that month as well. We will try to schedule each of the lab and exercise tests to be done following your ovulation date in that month.

Risks and Inconveniences

During the blood draw, you may feel slight pain from the needle or experience some dizziness. You may also develop a temporary bruise where the needle was inserted. If there is any difficulty in obtaining the blood or if there is some medical reason why we cannot perform the blood test, you will discontinue the study.

There exists the possibility of certain changes occurring during the cardiopulmonary test. These include abnormal blood pressure; fainting; irregular, fast, or slow heart rhythm; and, in rare instances, heart attack, stroke, or death. Every effort will be made to minimize these risks by evaluation of preliminary information relating to the participant's health and fitness and by careful observations during testing. Emergency equipment and trained personnel are available to deal with unusual situations that may arise. Since this is a submaximal exercise test, the risks associated are those typical of any physical activity, and are low.

The risks associated with exercise training are those typical of any physical activity. All participants will have been carefully screened prior to the initiation of the exercise protocol to minimize the risk of adverse events. Participants will be required to present a note from a physician indicating medical clearance for exercise training.

Although we are currently unaware of any risks, there may be possible risks to the dietary intervention, such as previously unknown allergies.

Benefits

This study is not designed for your direct benefit. The primary benefit of this study will be to increase understanding of how dietary interventions and exercise influence cardiovascular health. The cardiorespiratory benefits of moderate exercise are well known. Any information that is important to the participant's health will, with the participant's permission, be transmitted to their physician.

Results

While blood tests are sometimes done for clinical purposes, the kind of blood test you will have as part of this study is for research purposes only. This means that they are not designed to provide clinical information that might be helpful to you or your doctor and they may not show problems that would normally be found in a blood test ordered to evaluate a specific medical problem. If significant abnormalities are detected, you, or a physician whom you may designate, will be informed by a phone call.

Confidentiality

Your participation in this study will be confidential and if the results are published, your name will not be identified. Your records will be kept in locked files in locked offices and access will be allowed only to members of the research team or institutional personnel as part of a routine audit. Your name and other personal identifying information will be stored in an electronically secure database at Columbia University. Records will be available to research staff, and to Federal, State and Institutional regulatory personnel (who may review records as part of routine audits). The study could not be completed without this information. We will do everything we can to avoid disclosure about your participation in this study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as

required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Study Compensation
You will receive $25 for each blood draw, $25 for each submaximal exercise test, and $50 if you achieve 85% adherence to both the exercise and dietary arms of the study. In total, you could receive compensation of $250.

In Case of Injury
If you believe that you have sustained an injury as a result of participating in a research study, you may contact the Principal Investigator, Dr. Richard Sloan, at (646) 774 - 8940 so that you can review the matter and identify the medical resources that may be available to you.

In case of injury, New York State Psychiatric Institute will provide short term emergency medical treatment, which has been determined to be necessary by New York State Psychiatric Institute's doctors, and which is within the capability of New York State Psychiatric Institute to provide. In addition, we will provide assistance in arranging follow up care in such instances.

New York State Psychiatric Institute and Research Foundation for Mental Hygiene do not provide compensation or payment for treatment of research related injuries. However, you should be aware that you do not give up your legal right to seek such compensation through the court by participating in this research.

Please be aware that:

1. The New York State Psychiatric Institute, Columbia University and New York Presbyterian Hospital will furnish that emergency medical care determined to be necessary by the medical staff of this hospital.

2. You will be responsible for the cost of such care, either personally or through your medical insurance or other form of medical coverage.

3. No monetary compensation for wages lost as a result of injury will be paid to you by the New York State Psychiatric Institute, Columbia University or by New York Presbyterian Hospital.

4. By signing this consent form, you are not waiving any of your legal rights to seek compensation through the courts.

Questions
Research personnel will answer all current or future questions about the procedures and/or responses to the best of their ability. If you have any questions about this study in the future, you may reach Dr. Richard Sloan at 646-774-8940.

You will be notified of significant new findings that may relate to your willingness to continue to participate.

If you have any questions about your rights as a research participant, want to provide feedback, or have a complaint, you may call the NYSPI Institutional Review Board (IRB). (An IRB is a committee that protects the rights of human subjects in research studies). You may call the IRB Main Office at (646)774-7155 during regular office hours.

Documentation of Consent
I voluntarily agree to participate in the research study described above. I have received a copy of this consent form. I have been informed that if I believe I have sustained injury as a result of participating in a research study, I may contact the Principal Investigator, Dr. Richard Sloan at (646) 774-8940 so that I can review the matter.

Please indicate which exercise program you wish to enroll in by checking the appropriate box:

[ ] I wish to enroll in the PlusOne-based exercise program.

[ ] I wish to enroll in the home-based exercise program.

Print name: _____

Signed: _____ Date: _____

I have discussed the proposed research with this participant including the risks, benefits, and alternatives to participation (including the alternative of not participating in the research). The participant has had an opportunity to ask questions and in my opinion is capable of freely consenting to participate in this research.

Print name: _____
Person Designated to Obtain Consent

Signed: _____ Date: _____

HIPAA Form A

HIPAA Clinical Research Authorization for Sponsored Research

Protocol Number:
Name of Study: The Anti-Inflammatory Effects of Exercise and Peanut Consumption
Principal Investigator: Dr. Richard P. Sloan

For the purpose of the conduct of the above name study, I agree to permit Columbia University Medical Center, my doctors and my other health care providers (together "providers"), and Dr. Richard P. Sloan and his/her staff (together "Researchers"), to use and disclose health information about me as described below.

1. **The health information that may be used and disclosed includes:**
   - all information collected during the research described in the Informed Consent Form for the above-named study ("the research"); and
   - health information in my medical records that is relevant to the Research.
   - This may include medical history information that may be considered sensitive, including:

2. **The providers may disclose health information in my medical records to:**
   - the Researchers;
   - representatives of government agencies, review boards, and other persons who watch over the safety, efficacy, and conduct of the research.
     safety, effectiveness, and conduct of the research.

3. **The researchers may use and share my health information:**
   - among themselves and with other participating researchers to conduct the Research;
   - representatives of government agencies, review boards, and other persons who watch over the safety, effectiveness, and conduct of research; and
   - as permitted by the Informed Consent Form.

4. **The Sponsor may use and share my health information as permitted by the Informed Consent Form.**

5. **Once my health information has been disclosed to a third party (e.g., a pharmaceutical company participating in this Study), federal privacy laws may no longer protect it from further disclosure.**

6. **Please note that:**
   - You do not have to sign this Authorization, but if you do not, you may not participate in the Research.
   - You may change your mind and revoke (take back) this authorization at any time and for any reason. To revoke this Authorization, you must write to:

Dr. Richard P. Sloan
Behavioral Medicine Program,
Dept. of Psychiatry Columbia University Medical
Center 622 West 168th Street, Suite 1540
NY, NY 10032

. However, if you revoke this Authorization you will not be allowed to continue part in the Research. Also, even if you revoke this Authorization, the Researchers and the Sponsor may continue to use and disclose the information they have already collected as permitted by the Informed Consent Form

. While the Research is in progress, you may not be allowed to see your health information that is created or collected by Columbia University in the course of the Research. After the Research is finished, however, you may be allowed to see this information.

7. This Authorization does not have an expiration (ending) date.

8. You will be given a copy of this Authorization after you have signed it.

Printed Name of Subject: _____

Signature of Subject or Legal Representative: _____ Date: _____

Relationship of Legal Representative to Subject (if applicable): _____

New York State Psychiatric Institute (NYSPI)
Authorization to Use or Disclose Health Information during a Research Study

Protocol Number: 7466 **Principal Investigator:** Dr. Richard P. Sloan, Ph.D.

Name of Study: The Anti-Inflammatory Effects of Exercise and Peanut Consumption

Before researchers can use or share any identifiable health information ("Health Information") about you as part of the above study (the "Research"), the New York State Psychiatric Institute (NYSPI) is required to obtain your authorization. You agree to allow the following individuals and entities to use and disclose Health Information about you as described below:

- New York State Psychiatric Institute (NYSPI), your doctors and other health care providers, if any, and
- The Principal Investigator and his/her staff (together "Researchers"). Researchers may include staff of NYSPI, the New York State Office of Mental Health (OMH), Research Foundation for Mental Hygiene, Inc. (RFMH), and Columbia University (CU), provided such staff is a part of the study, and
- Providers of services for the Research at CU, NYSPI and/or RFMH, such as MRI or PET, or Central Reference Laboratories (NKI), if indicated in the consent form**.**

1. The Health Information that may be used and/or disclosed for this Research includes:

☑ All information collected during the Research as told to you in the Informed Consent Form.
☑ Health Information in your clinical research record which includes the results of physical exams, medical and psychiatric history, laboratory or diagnostic tests, or Health Information relating to a particular condition that is related to the Research.
☐ Additional information may include:

2. **The Health Information listed above may be disclosed to:**
☑ Researchers and their staff at the following organizations involved with this Research:
Columbia University Medical Center

☐ The Sponsor of the Research,

and its agents and contractors (together, "Sponsor"); and
☑ Representatives of regulatory and government agencies, institutional review boards, representatives of the Researchers and their institutions to the level needed to carry out their responsibilities related to the conduct of the research.
☐ Private laboratories and other persons and organizations that analyze your health information in connection with this study

☐ Other (family members or significant others, study buddies, outside agencies etc.) Specify:

3. By giving permission to release your Health Information as described above, you understand that your Health Information may be disclosed to individuals or entities which are not required to comply with the federal and state privacy laws which govern the use and disclosure of personal Health Information by NYSPI. This means that once your Health

Information has been disclosed to a third party which does not have to follow these laws (e.g., a drug company or the Sponsor of the Research), it may no longer be protected under the HIPAA or NYS Mental Hygiene Law requirements but is subject to the terms of the consent form and may be subject to other state or federal privacy laws or regulations.

4. **Please note that:**
   - You do not have to sign this Authorization form, but if you do not, you may not be able to participate in the study or receive study related care. You may change your mind at any time and for any reason. If you do so, you may no longer be allowed to participate in the study. If you withdraw this Authorization the research staff and the Sponsor, if this is sponsored research, may still use or disclose Health Information containing identifying information they already have collected about you as needed to maintain the reliability of the research. Any request to withdraw this Authorization must be made in writing to (enter name and contact information below):

     Dr. Richard Sloan, Ph.D. 622 West 168th Street, PH Suite 1540, New York, NY 10032
     Tel: 646-774-8940 Email: rps7@cumc.columbia.edu
   - While the Research is going on, you may not be allowed to review the Health Information in your clinical research record that has been created or collected by NYSPI. When this research has been completed you may be allowed to see this information. If it is needed for your care, your Health Information will be given to you or your Doctor.

5. **This Authorization does not have an end date.**

6. **You will be given a copy of this form after you have signed it.**

I agree to the use and disclosure of Health Information about me as described above:

_____ _____

Signature of Participant/ Legal Representative Date

_____

Printed Name of Participant

_____

Relationship of Legal Representative to Participant (if applicable)

We also ask you or your legal representative to initial the statements below:

☐ **I have received a copy of the NYSPI/OMH Notice of Privacy Practices.**

New York State Psychiatric Institute Institutional Review Board
Request for HIPAA Waiver of Authorization and/or
Waiver of Consent

Use this form if you are requesting to waive or alter <u>some or all</u> of the elements of consent and/or of HIPAA authorization requirements.

IRB Protocol Number 7466 Name of Principal Investigator Richard P. Sloan

Title of Study The Anti-Inflammatory Effects of Exercise and Peanut Consumption

Please indicate and explain nature of request below:

☒ Partial Waiver for telephone screens.

☐ Partial Waiver for internet survey research.

☐ Full Waiver for the purpose of accessing an existing database or records (paper or electronic) to identify potential subject or to conduct above research.

Describe the identifiable information that you will be collecting or accessing under this waiver (**Be specific to allow the IRB to determine whether the information includes any of the 18 HIPAA identifiers or any other method of identifying the individuals):** name, address, phone number, email address

The study, or phase of the study for which the waiver is being sought, should present no more than minimal risk to the subject, including risk to their confidentiality. Please explain how your study, or the phase of the study for which the waiver is being sought, meets the following criteria:

1. Explain why the waiver or alteration will not adversely affect the rights and welfare of the subjects. The information collected in the phone screen will not compromise the privacy of the screened subjects.

2. Explain why is it not practical to obtain consent and/or authorization from subjects? It will be impractical for us to ask subjects to come to our offices to sign a consent form and only then proceed to establish if they are eligible.

3. Can the research practicably be conducted without access to, and use of, the individually identifiable information? If not, why? Without this information, we will not be able to initiate the screening procedure.

4. Indicate how you plan to protect the identifiers from improper use and disclosure. Check all that apply:
   ☒Electronic safeguards where only study staff has access and the database meets all security requirements as outlined in the NYSPI Security Plan (e.g.

password protection, data encryption, firewall, no outside transmission of data, restricted access etc).

☐Physical safeguards where only study staff has access to areas with study information and NYSPI recommendations for physical security are in place (locked cabinets, locked filing room, restricted access etc).

☐No identifiers, links or codes will be retained that permit data to be identified.

☐Other:

5. Describe your plan to destroy the identifiers at the earliest opportunity:

   ☐Identifiers will be destroyed if the patient does not meet criteria for admission to the study

   ☐Identifiers will be retained until potential subjects sign consent and authorization and complete the study. Destruction of all identifiers will be consistent with federal, state and Institute policies, and or other contractual agreements.

   ☒ N/A as I will not record identifiers or create links or codes to connect the data

6. Where applicable: Describe how subjects will be provided with additional pertinent information after participation. N/A

By submitting this application you are certifying that the protected health information or other identifiable information will not be reused or disclosed except as required by law, for authorized oversight of the research, or for other research that has been reviewed and approved by the IRB with specific approval regarding access to this protected health information.

☒Agree ☐Do not agree

FOR THOSE REQUESTING ACCESS TO MEDICAL RECORDS MAINTAINED AT NYSPI

Please also complete the following to describe selection criteria for your request:

Selection Criteria for records required (e.g. diagnosis, age, date of admission)

Dates of required records: from / / through / /

Anticipated sources of information (check all that apply)

☐ Paper medical records, Owner

☐ OMH EMR and/or DUKE EMR

☐ Other (describe)

Number of records needed: Number _____ ☐ ≥ 50 ☐ < 50
