Official Title:	DISCOVER: A single-site double-blind placebo-controlled randomized mechanistic crossover trial to assess the influence of boDy weIght on aSpirin-triggered speCialized prO-resolVing mEdiatoRs
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NYU Langone Health

Research Subject Informed Consent Form

Title of Study:	DISCOVER: A single-site double-blind placebo-controlled randomized mechanistic crossover trial to assess the influence of bo**D**y we**I**ght on a**S**pirin-triggered spe**C**ialized pr**O**-resol**V**ing m**E**diato**R**s S20-01884
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1. About volunteering for this research study

You are being invited to take part in a research study. Your participation is voluntary which means you can choose whether or not you want to take part in this study.

People who agree to take part in research studies are called “subjects” or “research subjects”. These words are used throughout this consent form. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. You may also decide to discuss this study and this form with your family, friends, or doctor. If you have any questions about the study or about this form, please ask us. If you decide to take part in this study, you must sign this form. We will give you a copy of this form signed by you for you to keep.

2. What is the purpose of this study?

Aspirin is commonly used to prevent heart attacks and strokes in clinical care. Commonly a “baby” aspirin (81mg) is prescribed for this purpose. However, higher doses may work better in individuals who weigh more. This study will investigate how body weight influences aspirin’s ability to reduce inflammation. Aspirin is Food and Drug Administration (FDA) approved for the temporary relief of minor aches and pains, to temporarily reduce fever, and to reduce the chances of a heart attack, stroke and death in people with severe atherosclerosis. In this research study, the use of aspirin is considered ‘off-label’ and therefore investigational.

3. How long will I be in the study? How many other people will be in the study?

Your involvement will last approximately 12 weeks. We anticipate that the study will last about 3.5 years and include 125 subjects.

4. What will I be asked to do in the study?

You will attend 5 visits at the NYU-HHC CTSI Clinical Research Center. At each visit, you will have your blood pressure and body weight checked, complete questionnaires, and have your blood drawn. We will collect 50mL (just over 3 Tablespoons) each time blood is drawn. The blood will be taken to a lab and tested to study how aspirin affects inflammation.

During the study, you will be given capsules containing aspirin 81mg, aspirin 325mg, or placebo. Placebo looks just like aspirin but contains no active ingredients.

You will have two placebo “washout” periods (to make sure any effect of aspirin is out of your system) and two aspirin periods while in this study. Whether you receive the low-dose (81mg or high-dose 325mg) first is determined randomly (by chance, like flipping a coin). Everybody in the study will take 81mg aspirin for part of the study, 325mg aspirin for part of the study, and placebo for part of the study. However, you will not know whether you are receiving aspirin or placebo. Your doctor can find out in the event of an emergency. You will take one capsule daily between visits. You will be asked to bring your study medication (aspirin or placebo) with you to each visit, including any empty bottles.

You will also undergo a non-invasive vascular function test of the blood vessels under the tongue (glycocalyx) at each study visit. This involves a handheld clinical video microscope which is positioned under the tongue for 2-3 minutes which uses a processing software to evaluate microvascular health. The video microscope is not FDA approved and will be used on a research basis to collect physiologic data. The individual who will be performing this function test will follow the proper COVID 19 risk mitigation procedures.

Baseline Visit: 3 weeks before Visit 1, time: 1 hour

- Informed Consent
- Limited Medical History
- Questionnaires: food frequency (link provided), activity/exercise (may be completed any time)
- Food diary
- Medication/supplement review
- Blood pressure and body weight measurements
- Blood draw
- Sidestream darkfield imaging of glycocalyx
- Participant instructions and schedule for next visit
- Dispense capsules

Visit 1: 3 weeks after Baseline Visit, time: 1 hour

- Pill count
- Blood pressure and body weight measurements
- Blood draw
- Sidestream darkfield imaging of glycocalyx
- Adverse event monitoring
- Participant instructions and schedule for next visit
- Dispense capsules

Visit 2: 3 weeks after Visit 1, time: 1 hour

- Pill count
- Blood pressure measurements
- Blood draw
- Sidestream darkfield imaging of glycocalyx
- Adverse event monitoring
- Participant instructions and schedule for next visit
- Dispense capsules
- Body weight measurement on a special scale (bioelectrical impedance) to test body fat percentage
- Dual x-ray absorptiometry (a type of X-ray also known as a DEXA scan) to test body fat percentage

Visit 3: 3 weeks after Visit 2, time: 1 hour

- Pill count
- Blood pressure and body weight measurements
- Blood draw
- Sidestream darkfield imaging of glycocalyx
- Adverse event monitoring
- Participant instructions and schedule for next visit
- Dispense capsules

Visit 4: 3 weeks after Visit 3, time: 1 hour

- Pill count
- Blood pressure and body weight measurements
- Blood draw
- Sidestream darkfield imaging of glycocalyx
- Adverse event monitoring

Identifiers will be removed from the identifiable blood samples. After such removal the blood samples may be used for future research studies or shared with other researchers and we will not request additional informed consent from you to use these specimens as we have noted here.

5. What are the possible risks or discomforts?

Risk of Study Drug

Aspirin may cause severe allergic reactions in very rare instances. Aspirin, primarily 325mg, can cause gastritis (stomach inflammation) and gastrointestinal bleeding (bleeding in the stomach and intestine). The risk of these side effects are increased in those age >70 years, with a history of ulcers, bleeding disorders, concomitant use of an anti-platelet, anti-coagulant drug (to prevent clots), corticosteroids or other non-steroidal anti-inflammatory drug (NSAIDs), and heavy alcohol consumption.

It is possible, albeit unlikely, that use of aspirin may involve risks that are currently unforeseeable.

Other Risks

During this study, you will have exposure to radiation from dual x-ray absorptiometry. This radiation exposure is not necessary for your medical care and is for research purposes only. This means that you will be exposed to small doses or amounts of radiation. The risk from this amount of radiation is less than the risk from everyday exposure to the sun. The risks of receiving very small doses of radiation are thought to be low. These risks are not actually known.

Blood draws may cause brief pain or discomfort from the needle stick as well as temporary redness, bruising, or bleeding at the site of the needle insertion. Rarely, infection may occur. Some people feel faint from blood draws. If you feel faint, please tell the study team immediately.

Sidestream darkfield imaging is a technique used to assess blood flow in small vessels. It is performed with a clinical video microscope positioned under the tongue. Image acquisition takes 2-3 minutes. Holding a microscope under the tongue for 3 minutes may be associated with mild discomfort, although the video microscope itself is not expected to confer any additional risks. If you experience discomfort and feel that it is intolerable, the procedure will be stopped.

6. Can I be in the study if I am pregnant or breastfeeding?

If you are currently pregnant, you will not be able participate in the study. You should not become pregnant while you are participating in this study. If you are able to become pregnant, you will be required to use a medically accepted method of birth control while you participate in the study:

- Hormonal methods like birth control pills, patches, vaginal rings or implants,
- Barrier methods such as condoms or a diaphragm used with spermicide (a foam, cream or gel that kills sperm),
- Intrauterine device (IUD),
- Abstinence (no sex).

If you are capable of becoming pregnant, you will be asked for the date of your last menstrual period at each visit. If your period is late, you will have a pregnancy test at your visit to confirm that you aren't pregnant.

If you become or you think you have become pregnant during the study, you must tell the principal investigator right away and must tell your obstetrician or other health care provider caring for you during your pregnancy that you took part in this study. If you become pregnant, you will have to stop taking part in the study for safety reasons. The principal investigator may ask you to provide information about the outcome of your pregnancy and the health of your baby.

7. What if new information becomes available?

During the course of this study we may find more information that could be important to you.

This includes information that might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

8. What are the possible benefits of the study?

You are not expected to get any benefit from being in this research study. Individuals with obesity and/or cardiovascular disease may benefit in the future from what we learn in this study.

9. What other choices do I have if I do not participate?

You may qualify for other research studies that are of interest to you.

10. Will I be paid for being in this study?

You will be paid at the completion of study Visits 0, 1, 2, 3 and 4. If you adhere to the study medication, you will receive $40, $50, $50, $50, and $60, respectfully, at the completion of these visits. Additionally, upon completion of the food diary and dietary survey, you will receive $50.

If you complete all the study visits and are adherent to the treatment, you will receive $300.

As is required by the laws that apply to NYU Langone, in order for you to receive a payment you need to give the study staff either your Social Security number or your Alien Registration number and will be asked to complete a IRS W9. If you do not have either of these numbers or are not willing to complete the IRS, you may be in the study but will not receive any payment.

You are required to track all payments made to you by NYU Langone for your participation in any research for this calendar year. You must let us know immediately if/when the total research payments presently equal or is likely to exceed $600.00 total (not including travel reimbursements) for this calendar year. If your total payments (for one or more studies) reach $600.00, please advise Dr. Sean Heffron.

In order to receive payments for your participation in research, you may need to provide your Social Security number. This is because NYU Langone is required to report to the Internal Revenue Service (IRS) any amounts that are paid to research participants that are equal to or greater than $600.00, and you may be taxed on these research payments above $600.00. If you will receive payments in any amount by a check, you will need to provide your Social Security number or Alien Registration number and will be asked to complete an IRS W9. If you do not have either of these numbers or are not willing to complete the IRS W9, you may be in the study but will not receive any payment.

You will receive reimbursement for transportation costs for public transportation or parking (up to three hours) for study visits. In order to be reimbursed, you must give the receipts to the study staff.

11. Will I have to pay for anything?

You will not have to pay for anything associated with participating in this research study.

12. What happens if I am injured from being in the study?

For medical emergencies contact 911. If you think you have been injured as a result of taking part in this research study, tell the principal investigator as soon as possible. The principal investigator's name and phone number are listed at the top of page 1 of this consent form.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the NYU School of Medicine or Medical Center to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

13. When is the study over? Can I leave the study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped or your participation ended at any time by your physician or the National Institutes of Health (NIH) without your consent because:

- The principal investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The study sponsor (NIH) or the principal investigator has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. Leaving the study will not interfere with your future care, payment for your health care or your eligibility for health care benefits.

14. How will you protect my confidentiality?

Your medical information is protected health information, or "PHI", and is protected by federal and state laws, such as the Health Insurance Portability and Accountability Act, or HIPAA. This includes information in your research record as well as information in your medical record at NYU Langone Health. In compliance with NYU Langone Health policies and procedures and with HIPAA, only those individuals with a job purpose can access this information.

Medical information created by this research study may become part of your medical record. We may include your research information in your medical record for several reasons, including for the billing of services provided in connection with the study, to securely document any medical services you receive, and so that other members of the NYU Langone Health community who may treat you have access to important information about your health.

You have a right to access information in your medical record. In some cases, when necessary to protect the integrity of the research, you will not be allowed to see or copy certain information relating to the study while the study is in progress, but you will have the right to see and copy the information once the study is over in accordance with NYU Langone Health policies and applicable law.

To help us further protect your confidentiality, this research is covered by a Certificate of Confidentiality from NIH. The NIH has issued a Certificate of Confidentiality for this research. This adds special protection for the research information (data, documents, or biospecimens) that may identify you.

Research information protected by this Certificate of Confidentiality cannot be disclosed to anyone else who is not connected with the research, without your consent. With this Certificate of Confidentiality, the researchers may not disclose or use research information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, without your consent. However, disclosure, without your consent, is still necessary if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases). The Certificate of Confidentiality cannot be used to refuse a request for information from appropriate government agencies responsible for project oversight.

The Certificate of Confidentiality does not prevent you from releasing information about yourself and your involvement in this research, including for your medical treatment. Federal regulations may also allow for the use or sharing of information for other scientific research.

15. HIPAA Authorization

As noted in the Confidentiality section above, federal law requires us, and our affiliated researchers, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions. We are asking for your permission (authorization) to use and share your health information with others in connection with this study- in other words, for purposes of this research, including conducting and overseeing the study.

Your treatment outside of this study, payment for your health care, and your health care benefits will not be affected even if you do not authorize the use and disclosure of your information for this study.

What information may be used or shared with others in connection with this study?
All information in your research record for this study may be used and shared with those individuals listed in this section. Additionally, information in your medical record that the research team believes may be important to the study may be accessed by those listed here. This includes, for example, results from your physical examinations, laboratory tests, procedures, questionnaires, and diaries.

Who may use and share information in connection with this study?
The following individuals may use, share, or receive your information for this research study:

- The research team, including the Principal Investigator, study coordinators, and personnel responsible for the support or oversight of the study
- The study sponsor: NIH
- Governmental agencies responsible for research oversight (e.g., the Food and Drug Administration or FDA)
- Data & Safety Monitoring Board
- H+H personnel responsible for the support or oversight of the study at Bellevue Hospital

Your information may be re-disclosed or used for other purposes if the person who receives your information is not required by law to protect the privacy of the information.

What if I do not want to give permission to use and share my information for this study?
Signing this form is voluntary. You do not have to give us permission to use and share your information, but if you do not, you will not be able to participate in this study.

Can I change my mind and withdraw permission to use or share my information?
Yes, you may withdraw or take back your permission to use and share your health information at any time for this research study. If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. To withdraw your permission, send a written notice to the principal investigator for the study noted at the top of page 1 of this form. If you withdraw your permission, you will not be able to stay in this study.

How long may my information be used or shared?
Your permission to use or share your personal health information for this study will never expire unless you withdraw it.

16. The Institutional Review Board (IRB) and how it protects you

The IRB reviews all human research studies – including this study. The IRB follows Federal Government rules and guidelines designed to protect the rights and welfare of the people taking part in the research studies. The IRB also reviews research to make sure the risks for all studies are as small as possible. The NYU IRB Office number is (212) 263-4110. The NYU School of Medicine's IRB is made up of:

- Doctors, nurses, non-scientists, and people from the community

17. Who can I call with questions, or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on top of the page 1 of this consent form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Institutional Review Board (IRB) at (212) 263-4110.

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 web site at any time.

18. Optional storage of leftover blood samples for future research

With your permission, we would like to store any leftover blood samples for future research related to cardiovascular disease, inflammation and immune dysfunction, including its complications, and to improve treatment. This is optional, meaning your decision regarding your leftover blood samples will not impact your ability to be in this study.

Your samples will be labeled with a unique code and stored indefinitely in Dr. Heffron's laboratory. Dr. Heffron will keep a special key that will connect this unique code with your identifiable information in a separate, secure location. We will not perform genetic tests on your samples (to determine whether you are at risk for developing a genetic disease). The results of these research tests will not be shared with you.

If you decide to allow us to store your samples and later change your mind, you can request the destruction of any remaining samples by writing to Dr. Heffron at any time.

Please mark your initials next to one of the options below:

____YES: I consent to the storage of my leftover samples for future research.

____NO: I DO NOT want my leftover samples stored for future research

When you sign this form, you are agreeing to take part in this research study as described to you. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer.

Name of Subject (Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date

Witness to Consent Process for Non-English-Speaking Subjects (using a translated consent form OR "Short Form" in Subject's Spoken Language)

Statement of Witness

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

Name of Witness (Print)	Signature of Witness	Date