The Children's Hospital *of* Philadelphia®

Informed Consent Form and HIPAA Authorization

Study Title: Cardiometabolic risk and obesity in adolescents with Down syndrome

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Division of Endocrinology

You, or your child, may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research study, and the risks and possible benefits of participating.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this study if you do not want to. If you take part, you can leave the study at any time.

In the sections that follow, the word "we" means the study doctor and other research staff. If you are a parent or legal guardian who is giving permission for a child, please note that the word "you" refers to your child.

Why are you being asked to take part in this study?

You are being asked to take part in this research study because you are between the ages of 10 – 20 years old. You either have Down syndrome or you are being asked to participate as a control subject.

What is the purpose of this research study?

The purpose of this research study is to determine which measures best capture cardiovascular disease risk and type 2 diabetes risk in children and adolescents with Down syndrome.

How many people will take part?

About 250 people will take part in this study. This study is taking place at two locations: Children's Hospital of Philadelphia in Philadelphia, PA and Children's National Medical Center in Washington, DC. 202 people will participate at Children's Hospital of Philadelphia, and 48 people will participate at Children's National Medical Center.

What is involved in the study?

If you agree to take part, your participation will involve 1 study visit that can last approximately 5-8 hours. Participation in this study would also require answering some questions about your diet on 3 separate occasions after your visit and wearing a physical activity armband for 7 days in a row after the study visit.

Study Procedures

If you take part in this study you will have the following tests and procedures.

Interview: A team member will take your complete medical history, along with a listing of any medications you are taking. Throughout the study, you will be asked to report if you think that anything bad has happened as a result of the study.

Medical Record Review: Your medical record will be looked at by the study coordinator or the study doctors. The purpose of this medical record review is to ensure that we do not miss any major medical events, and that we get accurate information about the duration of any illness or medication use. Relevant clinical lab results from this study will be in your medical record.

Physical Exam: Your blood pressure, height, weight, skin-fold thickness and waist will be measured. A doctor will also examine your private areas to check how you are developing there.

Overnight Fast: You will not be able to eat or drink anything except plain unflavored water after 10:00 PM the night before your study visit. If you are not receiving an Oral Glucose Tolerance Test (OGTT), you will be allowed to eat after the fasting blood draw is complete. If you are receiving an OGTT, you will be allowed to eat after the OGTT is complete.

Fasting blood sample*: A blood sample will be drawn to check sugar, lipids, and other factors. About 2½ teaspoons of blood will be drawn.

Urine Pregnancy Test*: If you are female, you will be asked to take a pregnancy test before starting the study. The result will be shared with you and not with your parent(s), unless you give us permission to do so. The investigators will strongly encourage you to share the result with your parent(s). If you are found to be pregnant, you will not be able to participate in this study.

Oral Glucose Tolerance Test (OGTT)*: This test tells how well your body deals with sugar. The OGTT will be done only for participants with a BMI greater than or equal to the 85th percentile. Your BMI percentile is _____.

☐ You will have an OGTT.

☐ You will not have an OGTT

The test includes placement of an intravenous (IV) line in your arm/hand to make taking the blood samples easier. With the IV in place, you will not need to be stuck again for any further blood draws.

If you prefer, a numbing cream can be placed on your skin for about 45 minutes before this test to numb the area. Once the IV is in place, you will receive a sugar drink (Glucola) that tastes like a very sweet flat soda. You will have about 2 minutes to finish the drink. Over the next 2 hours, blood will be drawn 4 more times from your IV line. The total amount of blood drawn for the OGTT will be about 1½ teaspoons.

*In order to analyze the blood and urine samples you provide us with, some information will be shared with the University of Pennsylvania and Liposcience, Inc. These groups will only have access to dates; they will not have access to your name or other readily identifiable information.

DXA Scan: A special x-ray of the body called a DXA scan will be done to measure the amount of fat and lean (non-fat) tissue in your body. During the DXA scan, you will be asked to lie flat on your back on a table as the scanning machine moves above your body. The DXA scan is like an X-ray, and takes about 5-10 minutes. This test is painless and does not involve any needles.

Pulse wave velocity/Pulse wave analysis (Ultrasound): An ultrasound probe and cuff will track how fast your blood flows between your (neck) carotid artery and (thigh) femoral artery. You will lay on an examination table for the test, which should last for about 30 minutes. This test is painless and does not involve needles.

Echocardiography (Ultrasound): You will receive an ultrasound of your heart. You will remove your clothing from your upper body and will be covered by a gown or sheet to keep you comfortable and cover your private areas. You will lay on an examination table for the test. A colorless gel will be applied to your chest and a patch that will pick up signals electronically will be placed on your chest over the gel area. This test is painless and does not involve needles. This test should last about 45 minutes.

Questionnaires: During the study visit, a member of the study team will guide you through filling out questionnaires. Our staff person will read each survey out loud to you and you will let that person know your answers.

Procedures that take place at Home:

Diet Assessment: After you complete the study visit, a nutritionist will be in contact with you by phone/email to record the type/amount of food/drinks you ate during the last 24 hours. This will be done 3 times (2 times to report on weekdays and 1 time for a weekend day).

Physical Activity Armbands and diary: At the end of the study visit, you will be asked to take home and wear an armband. This armband is to be worn for 7 days straight, with the exception of bathing/showering or if participating in water activities, such as swimming. Wearing this armband measures your daily physical activity. You will also be asked to complete a physical activity diary.

After the 7th day, this armband and diary will be returned to the study team.

How long will you be in this study?

If you agree to take part, your participation will last for approximately 5 to 8 hours and will involve 1 study visit. You will also be asked to answer questions about your diet on 3 separate occasions after you have completed your study visit and to wear a physical activity armband for 7 days in a row after your visit.

Visit Schedule

The table below provides a brief description of the purpose, the main procedures and the duration of each study visit.

Visit	Purpose	Main Procedures	Duration
Visit 1	Baseline Visit	Interview & Physical Exam Blood and pregnancy test, OGTT DXA scan Pulse wave velocity & analysis Echocardiography, Questionnaires	5-8hours
Home	Diet Recall (done on 3	Dietary Assessement	30 minutes

	separate days)		
Home	Physical Activity Level	Physical activity armbands and diary	7 days

What are the risks of this study?

Your health is important to us. Taking part in a research study involves inconveniences and risks. If you have any questions about any of the possible risks listed below, you should talk to your study doctor or your regular doctor.

While in this study, you are at risk for the following side effects:

Risks associated with overnight fast:

You will be participating in this study after an overnight fast of 8-12 hours. You will not be eating breakfast before your blood draw on the day of the study and this may cause you to have an upset stomach, a headache, or feel light-headed. These symptoms are occasional but not serious. If you are not receiving an OGTT, you will be allowed to eat after the fasting blood draw is complete. If you are receiving an OGTT, you will be allowed to eat after the OGTT is complete.

Risks associated with blood draw:

There is a small and rare risk of infection and fainting. There may be some pain or bruising of the skin at the site where the blood is taken. The blood samples will be drawn by a health professional skilled in drawing blood in children and adolescents.

Risk associated with oral glucose tolerance test:

There is a small and rare risk of an upset stomach when drinking the sugar drink. Some people feel lightheaded, dizzy, shaky or sweaty during this test.

Risks associated with growth and maturity status and body composition:

Taking measurements of the body to determine growth and body compositions poses little risk. It is possible that you may experience some embarrassment when your pubertal status is determined. To minimize this possibility, the exam is done in private by a health professional skilled in determining pubertal status. In addition, you will be asked in advance if you prefer to have your parent/guardian present when the puberty exam is done.

Risks associated with DXA scan:

This study involves a very small exposure to radiation from the DXA scan. You will therefore receive a radiation dose. This dose is not needed for your medical care. You will get the radiation only because you are taking part in this study. At doses much higher than you would receive in this study, radiation is known to increase the risk of developing cancer after many years. At the small dose of radiation you will receive, it is very likely that you will see no effects at all. The DXA scan involves radiation exposure which is less than a person would receive from a chest X-ray or a dental X-ray.

Risks associated with pulse wave velocity and analysis (ultrasound):

This non-invasive test uses sound waves and there is no radiation exposure. There are no known risks from the ultrasound.

Risk associated with echocardiography (ultrasound):

This non-invasive test uses sound waves and there is no radiation exposure. There are no known risks from the ultrasound.

Risk associated with questionnaires:

Sensitive issues may arise during the questionnaire assessment. A licensed clinical psychologist who is part of the study team will be available for support, if needed. You do not have to answer any questions that make you uncomfortable.

Risk associated with wearing the physical activity armbands:

There is little to no risk associated with wearing the physical activity armband. These armbands fit comfortably on the arm and can easily be removed should discomfort arise. There is a slight chance that the skin could be irritated from wearing the armband. If skin irritation occurs, you may use Aquaphor or Vaseline where the fabric of the band is to treat and prevent further irritation. If you are allergic to metal, you will not be required to complete this test.

Reproductive Risks

For female subjects: There may be risks from some of the study procedures to an unborn child. If you are pregnant or nursing, you will not be allowed to participate in this study.

Risks associated with breach of confidentiality:

As with any study involving collection of data, there is the possibility of breach of confidentiality of data. Every precaution will be taken to secure participants' personal information to ensure confidentiality.
At the time of participation, each participant will be assigned a study identification number. This number will be used on data collection forms, blood samples, and in the database instead of names and other private information. A separate list will be maintained that will link each participant's name to the study identification number for future reference and communication.

Are there any benefits to taking part in this study?

We cannot guarantee or promise that you will receive any direct benefit by participating in this study. The knowledge gained from this research may help doctors determine what would be the best measure for determining heart disease risk in adolescents with Down syndrome. The results from this study may be beneficial to the Down syndrome community.

If you undergo the oral glucose tolerance test, you might benefit by finding out if you have any abnormalities such as diabetes. From the other blood tests, you might indirectly benefit by finding out you have another abnormalities such as, abnormal cholesterol levels and/or hypothyroidism. If clinical abnormalities are found, you will be notified. With your permission, we can send the clinically relevant lab results to your doctor. There may be a delay in transmitting certain lab results, because certain labs need to be processed together.

Do you need to give your consent in order to participate?

If you decide to participate in this study, you must sign this form. A copy will be given to you to keep as a record. Please consider the study time commitments and responsibilities as a research subject when making your decision about participating in this study

What happens if you decide not to take part in this study?

Participation in this study is voluntary. You do not have to take part in order to receive care at CHOP.

If you decide not take part or if you change your mind later there will be no penalties or loss of any benefits to which you are otherwise entitled.

Can you stop your participation in the study early?

You can stop being in the study at any time. You do not have to give a reason.

Can the study doctor take you out of the study early?

The study doctors may take you off of the study if:

- You are pregnant.
- The study is stopped.
- You cannot meet all the requirements of the study.

What about privacy, authorization for use of Personal Health Information (PHI) and confidentiality?

As part of this research, health information about you will be collected. This will include information from medical records, procedures, interviews and tests, etc. Laboratory test results will appear in your medical record with the exception of: insulin levels, other labs not performed in the CHOP Clinical Lab, and ultrasound results. We will do our best to keep your personal information private and confidential. However, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results of this study may be shown at meetings and published in journals to inform other doctors and health professionals. We will keep your identity private in any publication or presentation.

Several people and organizations may review or receive your identifiable information. They will need this information to conduct the research, to assure the quality of the data, or to analyze the data or samples. These groups include:

- Members of the research team and other authorized staff at CHOP;
- Members of the research team at Children's National Medical Center
- People from agencies and organizations that perform independent accreditation and/or oversight of research; such as the Department of Health and Human Services, Office for Human Research Protections.

By law, CHOP is required to protect your health information. The research staff will only allow access to your health information to the groups listed above. By signing this document, you are authorizing CHOP to use and/or release your health information for this research. Some of the organizations listed above may not be required to protect your

information under Federal privacy laws. If permitted by law, they may be allowed to share it with others without your permission.

There is no set time for destroying the information that will be collected for this study. Your permission to use and share the information and data from this study will continue until the research study ends and will not expire. Researchers continue to analyze data for many years and it is not possible to know when they will be completely done.

Can you change your mind about the use of personal information?

You may change your mind and withdraw your permission to use and disclose your health information at any time. To take back your permission, you must tell the investigator in writing.

Dr. Andrea Kelly
The Children's Hospital of Philadelphia
34th Street and Civic Center Blvd.
Philadelphia, PA 19104

In the letter, state that you changed your mind and do not want any more of your health information collected. The personal information that has been collected already will be used if necessary for the research. No new information will be collected. If you withdraw your permission to use your personal health information, you will be withdrawn from the study.

Financial Information

Will there be any additional costs?

The National Institute of Health (NIH) is providing financial support and material for this study. All procedures in this study will be covered. There are no costs to you or your health insurance.

Will you be paid for taking part in this study?

Parents/guardians will be reimbursed with a total of $100 on a prepaid bankcard for travel, meals and parking. The bank will have access to your name, address and phone number. $50 will be loaded onto the bankcard immediately after the study visit, and an additional $50 will be loaded once all at-home procedures are complete.

Participants will be compensated with a $50 gift card for their time and effort.

Who is funding this research study?

The National Institutes of Health is providing funding for this study.

What if you have questions about the study?

If you have questions about the study, call the study doctor, Dr. Kelly, at 215-590-3174, or the study coordinator at 267-426-2778.

You may also talk to your own doctor if you have questions or concerns.

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia has reviewed and approved this study. The IRB looks at research studies like these and makes sure research subjects' rights and welfare are protected. If you have questions about your rights or if you have a complaint, you can call the IRB Office at 215-590-2830.

Consent to share information with treatment study, "Levothyroxine treatment and cardiometabolic outcomes in adolescents with Down syndrome" (DS group only)

We are conducting another research study that will look at whether treating "subclinical hypothyroidism" in adolescents with DS improves their health. "Subclinical hypothyroidism" means that your body's level of thyroid stimulating hormone (TSH) is increased, but your thyroid hormone (T4) levels are normal. This treatment study would involve taking either levothyroxine for 12 months, or a placebo for 6 months followed by levothyroxine for 6 months. It will involve 3 additional study visits at CHOP Main that include all of the procedures done today, except for the PWV/PWA and Echocardiography. It would also involve 3 blood draw visits that can take place at any CHOP Satellite Clinic that is convenient for you.

If you give us permission, we will use your information from today's visit to screen you for the treatment study. We also may contact you to clarify some of the information that you provided at today's visit in order to determine that that you qualify for the treatment study.

Being screened does not mean that you must participate. If you qualify for the treatment study based on the information that we collect today, we will contact you and give you time to decide whether or not you want to participate.

Please indicate whether or not you will allow us to use your data from today's visit to screen you for "Levothyroxine treatment and cardiometabolic outcomes in adolescents with Down syndrome" by putting your initials next to one of the following choices:

_____ (initials) You may use my information from today's visit to screen me for the corresponding treatment study.

_____ (initials) I do not wish to be screened for the corresponding treatment study.

Consent for Use of Data for Future Research

As part of the study, we will collect data from you. We may wish to use this information in a future study about obesity, heart health, diabetes, or Down syndrome. The information will be given a unique code and will not include information that can identify you. Information that can identify you or your data may be kept permanently in a password protected computer database at CHOP. Only the study doctors and those working with them on this study will be able to see information that can identify you.

If you leave the study, you can ask to have the data collected about you removed. You can also ask us to remove information that identifies you from the data.

Please indicate whether you will allow your data to be used for future research in obesity, heart health, diabetes, or Down syndrome by putting your initials next to one of the following choices:

_____ (initials) My data may be used for other future research studies. If the data is shared outside of CHOP, no identifiable information will be included.

_____ (initials) My data may be used for this study only.

OPTIONAL: Consent to be contacted for future study

Please indicate if you will allow us to contact you for a future study.

_____ (initials) I give permission to be contacted for a future study.

_____ (initials) I do not wish to be contacted for a future study.

OPTIONAL: Consent to inform primary care physician of clinically relevant lab results

Please indicate if you will allow us to inform your primary care physician of any clinically relevant lab results.

_____ (initials) I give the study permission to inform my primary care physician of clinically relevant lab results.

_____ (initials) I do not wish for the study to inform my primary care physician of clinically relevant lab results.

Consent to Take Part in this Research Study and Authorization to Use and Disclose Health Information for the Research

The research study and consent form have been explained to you by:

Person Obtaining Consent	**Signature of Person Obtaining Consent** **Date:**

By signing this form, you are indicating that you have had your questions answered, you agree to take part in this research study and you are legally authorized to consent to your child's participation. You are also agreeing to let CHOP use and share your child's health information as explained above. If you don't agree to the collection, use and sharing of your child's health information, your child cannot participate in this study. **NOTE:** *A foster parent is not legally authorized to consent for a foster child's participation.*

Name of Subject	
Signature of Subject (18 years or older and competent to consent)	Date
Name of Authorized Representative (if different than subject)	Relation to subject: ☐ Parent ☐ Legal Guardian ☐ Legally Authorized Representative (subjects not competent to consent)
Signature of Authorized Representative	Date

Child Assent to Take Part in this Research Study

For children capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Obtaining Assent

_____ _____
Signature of Person Obtaining Assent Date

This study has been explained to me and I agree to take part.

_____ _____
Signature of Subject (optional) Date

For children unable to assent:

I certify that _____ was not capable of understanding the procedures involved in the study sufficiently to assent to study participation.

_____
Person Obtaining Assent

_____ _____
Signature of Person Obtaining Assent Date