COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: The effect of lactation on insulin sensitivity and lipolysis in women

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Research Study Summary:
We are asking you to join a research study. The purpose of this research study is to understand whether lactation amongst women with a history of gestational diabetes (GDM) improves metabolic health post-partum.

Study procedures will include: physical examination, blood work, an oral glucose tolerance test (like what is done during pregnancy), an insulin clamp, Continuous Glucose Monitoring (CGM), and DXA scan (described in more detail on the following pages).

Three visits are required. The first visit will take about 4 hours, the second visit will take about 15 minutes, and the third visit will take about 7 hours.

There are some risks from participating in this study. The main risks are associated with the IV placement that is required for the blood work, oral glucose tolerance test and the insulin clamp. These procedures are routinely performed by our experienced research staff and the most common risk is bruising or soreness at the site. The total amount of blood drawn for this study is 220 mL, and people who are in good health are not usually affected by this kind of blood loss. DXA scanning is also routinely performed by our research team and it is safe to use in lactating women.

The study may have no benefits to you. However, knowledge gained from the study will help us to better understand lactation and metabolic health.

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

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Why is this study being offered to me?
We are asking you to take part in this research study because you are a woman with a history of gestational diabetes who gave birth in the past 18 months. We are looking for 32 women to be part of this study.

Who is paying for the study?
The Yale Diabetes Research Center (DRC) and the National Institutes of Health (NIH) are sponsoring this study.

What is the study about?
The purpose of this study is to understand whether lactation amongst women with a history of gestational diabetes improves metabolic health post-partum. Specifically, we are looking at insulin sensitivity and fat utilization.

What are you asking me to do and how long will it take?
If you agree to take part in this study, this is what will happen:

For patients at Yale Medicine's Maternal-Fetal Medicine Clinic:

Post-partum OGTT visit (if applicable): If you are a patient at Yale Medicine's Maternal-Fetal Medicine Clinic, your doctor may ask you to have an oral glucose tolerance test (OGTT) 6-8 weeks after delivery as part of standard of care (not research-related). At this visit, a member of our research team will discuss this study with you and if you are interested in participating, we will ask you to complete questionnaires assessing your infant feeding practices. These can be completed on a computer or smart phone and will take about 20 minutes. If you are lactating, will have the option to provide us with 2-4 mL of expressed breastmilk so that we can study its contents, including milk lipids, protein, lactose and nucleic acids. The breastmilk will be stored for the duration of the study and will not be shared with anyone outside of this study.

Approximately 8 weeks later, you will be contacted by a research team member and asked about your infant feeding practices. Based on the information you provide, we will determine if you are eligible for the remainder of the study, and you may be invited to return for Visit 1, Visit 2 and Visit 3 (described below).

For women who are not patients at Yale Medicine's Maternal-Fetal Medicine Clinic:

Screening visit (Visit 1): You will arrive at the Yale New Haven Hospital (YNHH) Research Unit (HRU) or Church Street Research Unit (CSRU) after an overnight fast. You will be screened with a medical history, physical examination, blood work and a urine pregnancy test. An oral glucose tolerance test (OGTT) will be performed, like what is done during pregnancy. A nurse will insert an intravenous (IV) catheter into one arm and you will drink 7.5 ounces of glucola, which is a drink that contains 75 grams of glucose (sugar) in flavored water. Blood samples will be taken at certain time points before and after you drink the glucola. This visit will take about 4 hours.

Continuous Glucose Monitor (CGM) Placement (Visit 2): This visit will occur at the HRU or CSRU approximately 2 weeks prior to Visit 3. A trained study staff member will explain to you how to use the CGM (Dexcom G6 Pro) and will then insert the CGM's plastic wire-like tip under your skin with the use of the CGM applicator. This visit will take approximately 15 minutes. The

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CGM allows us to measure your interstitial sugar levels continuously throughout the day. We will ask you to wear the CGM for 10 days. It will be placed on your upper arm and attached with an adhesive patch. The sensor includes a wire-like tip which will be under your skin in your fat tissue. The sensor is sterile and comes in an unopened package. The sensor will be connected to a transmitter that captures and stores data from the sensor. The sensor/transmitterare single use only and disposable. The Dexcom G6 Pro does not require any calibration, as is the case with other CGM devices. There are no restrictions while you wear the transmitter/sensor with regard to physical activity except for swimming. Intense exercise may cause the sensor to loosen due to sweat or movement of the sensor. If the CGM sensor falls off while you are wearing it, we will ask you to return to the HRU or CSRU so that a new sensor can be re-inserted.

Insulin clamp and DXA scan (Visit 3):
After an overnight fast, you will return to the YNHH HRU. Two IV catheters will be inserted: one into each arm. Then, you will receive an infusion of insulin, the hormone that controls blood sugar levels, together with an infusion of [6,6-2H] Glucose and [2H5] Glycerol. The IVs will also be used to collect small blood samples every 5 minutes. The infusion rates will be variable to keep your blood sugar levels at ~90 mg/dl (this is a normal, healthy level). After the insulin clamp is completed, body composition will be assessed using a DXA scan. This visit will take about 7 hours.

At this visit, we will perform indirect calorimetry a total of 3 times (once before and twice during the insulin clamp). A transparent plastic hood will be placed over your head for 30 minutes each time. A hose connects the hood to a calorimeter, which measures your oxygen consumption and carbon dioxide production and calculates your resting energy expenditure.

Also at this visit, the CGM will be removed from your skin by a trained study staff member. To remove the sensor, the adhesive patch will be gently peeled off from the skin. Removal of the sensor is a painless procedure. The sensor and transmitter will be discarded after use.

Questionnaires: You will be asked to complete questionnaires assessing your infant feeding practices. These can be completed on a computer or smart phone at your convenience and will take about 20 minutes.

What are the risks and discomforts of participating?
Blood work, IV placement and phlebotomy: Blood work is a routine medical procedure. Study doctors and/or nurse practitioners will assess the screening blood work and if any abnormal findings occur they will provide you with appropriate medical advice. IV placement is also a routine medical procedure that is frequently performed by our experienced research staff and is done under sterile conditions. Risks include bruising or soreness at the site. If this occurs, appropriate treatment will be provided. On extremely rare occasions, a blood clot or infection might occur, and if this happens, you will be treated by medical personnel. You may also feel symptoms such as nausea, sweating or lightheadedness during the IV placement but this should resolve once the IV is placed. Phlebotomy (drawing blood) can result in anemia, although the amount of blood taken for this study should not result in anemia (~220mL total). You will be excluded from participating in the study if you have anemia based on screening blood work. You will also be advised to refrain from blood donation for 30 days after study completion.

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Oral glucose tolerance test (OGTT): The OGTT is a commonly used test for the diagnosis of type 2 diabetes and gestational diabetes. It is not associated with any specific risks. Occasionally, some participants may feel mild nausea or stomach discomfort after drinking the glucola; however, this typically resolves after eating food.

Insulin clamp: The infusion of insulin and glucose poses a small risk that your blood sugar will fall below the predetermined level (90 mg/dl) resulting in mild to no symptoms of low blood sugar including sleepiness, hunger, anxiety, sweating and shaking. These symptoms can be quickly reversed by infusing more glucose in the IV. To avoid this, your blood sugar levels will be checked every 5 minutes so that we can adjust the glucose infusion accordingly. The clamp will be performed under the supervision of a qualified physician or nurse practitioner. All infusions that are administered in the IV are sterile.

[6,6-2H] Glucose and [2H5] Glycerol: The infusion of [6,6-2H] Glucose and [2H5] Glycerol involves no radioactivity, and they are processed in your body the same as regular glucose and glycerol. These infusions have been used at Yale for decades with no side effects. The infusions are made by the Yale New Haven Hospital Investigational Drug Service (IDS) and are tested to be sterile before being administered.

Continuous glucose monitor (CGM): The CGM poses no major risks to the users. Some individuals may experience bruising and bleeding of the skin at the insertion site of the CGM sensor. This minor condition will resolve by itself in a few days. You may feel a mild discomfort (pin prick sensation) during the sensor insertion. Redness and discomfort (infection and inflammation) can occur at the sensor insertion site. Some individuals may be sensitive to the adhesive that keeps the sensor attached to the skin. If you notice significant skin irritation around or under the sensor, please contact us and we will remove the sensor. Rarely sensors may break and a small piece may remain under the skin which will need to be removed by the study physician. This may cause mild discomfort, bruising, or temporary bleeding. The Dexcom G6 Pro must be removed prior to Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, X-ray, or high-frequency electrical heat (diathermy) treatment

DXA scanning: DXA scanning is routinely performed by our research team and it is safe to use in lactating women. The amount of radiation you will be exposed to is small (one tenth of the amount of radiation for a chest X-ray).

Indirect calorimetry: Indirect calorimetry is routinely performed by our research team and poses no major risks to the users. Some people may feel claustrophobic and if this happens, we will remove the hood and stop the testing.

Questionnaires: The questionnaires are generally safe. The major inconvenience is the time taken to complete them and a possible breach of confidentiality. Your participation is voluntary and you are free to drop out at any time without penalty. All data will be kept confidential except in cases of imminent danger to you. Good clinical and research practice procedures and HIPAA regulations will be followed (described in more detail on the following pages). Your data will be assigned a study code, and you will not be identified by name in any of the published literature.

How will I know about new risks or important information about the study?

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We will tell you if we learn any new information that could change your mind about taking part in this study.

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How can the study possibly benefit me?
The study may have no benefits to you.

How can the study possibly benefit other people?
Knowledge gained from the study will help us to better understand lactation and metabolic health.

Are there any costs to participation?
You will not have to pay for taking part in this study. The only costs include transportation and your time coming to the study visits.

Will I be paid for participation?
You will be paid for taking part in this study as follows:

$50 for Visit 1
$15 for wearing the CGM
$100 for Visit 3
$20 for completing the questionnaires
$15 for providing expressed breastmilk (optional)
Parking vouchers for the study visits
Reimbursement for child care for the duration of the study visits (up to $15/hr)

. We will use a Bank of America pre-paid debit card to provide the payment for taking part in the study. We will have to share your name, address, and telephone number with Bank of America for ePayments. You will receive a card in the mail with the first payment. You will need to activate the card over the phone. Each additional payment will be automatically added to your card.

According to the rules of the Internal Revenue Service (IRS), payments that are made to you because of your participation in this study may be considered taxable income. You are responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments.

What are my choices if I decide not to take part in this study?
The alternative would be not to participate in the study.

How will you keep my data safe and private?

We will keep information we collect about you confidential. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if you we learn that you are hurting a child or an older person.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

It is important for you to know that if you do not already have a medical record at YNHH, one will be made for your visit. Some information related to the care given to you during study visits will become part of your Yale New Haven Hospital (YNHH) electronic medical record (EMR). For example, any laboratory test results that are sent to the YNHH lab for testing will appear in your

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medical record and any printed copies of your record. Once placed in the EMR, these results are accessible to all of your providers who participate in the EMR system. Information within your EMR may also be shared with others who are appropriate to have access to your EMR (e.g., health insurance company, disability provider.) In addition, you need to know that when any person is admitted to the YNHH, the individual's previous medical records of other visits or admissions to YNHH become available to physicians and hospital staff in order to ensure that the best possible care can be provided to the individual during the hospital stay. Similarly, the researchers and staff will have access to whatever information is already in your YNHH medical records such as past surgeries or medical conditions, emergency room visits, or possibly clinic visits. If such access to your past medical history by researchers and staff responsible for the study is unacceptable to you, then you should not participate in the research study.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name, date of birth, address and phone number. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify you will remain confidential.

All identifiable information that is obtained in connection with this study is stored in password protected secure computer data files and will remain confidential and will be disclosed only with your permission or as required by U.S. or State law. All of the information obtained in this study is kept in locked files and will be kept confidential. When the study is completed, subject information is stored at least for 7 years in locked cabinets within a locked storage unit that only the investigators of the study have access to. The link to your personal information will be kept for 7 years, after which time the link will be destroyed and the data will become anonymous.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens 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, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or

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program evaluation by NIH/NIDDK which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called "Protected Health Information." It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- The entire research record and any medical records held by YNHH from the time your medical record was created until present
- Records about your study visits
- Information will be collected on the infant (birth weight/percentile and weight/percentile at 2 months of age
- Information obtained during this research regarding
  - Medical history and physical exams
  - Laboratory and x-ray test results
  - Questionnaires
  - Breast milk analysis (optional)

How will you use and share my information?
We will use your information to conduct the study described in this consent form.

We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- National institutes of Health (NIH)
- Representatives from Yale University, the Yale Human Research Protection Program and the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
- The Principal Investigator
- The study sponsor
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team

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- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study

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We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and Yale-New Haven Hospital are required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Authorized representatives of the National Institutes of Health and the FDA may need to review records of individual subjects. People from the FDA or other Health and Human Services agencies may see your name, but they are bound by rules of confidentiality not to reveal your child's identity to others.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record.

What if I change my mind?

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to the principal investigator at the mailing address listed on page 1.

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to insure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?

If you are injured while enrolled in the study, seek treatment and contact the study team as soon as you are able. Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available.

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits. Not

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participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

What will happen with my data if I stop participating?
Data and samples will be unable to be withdrawn once they are collected and they will remain de-identified.

Who should I contact if I have questions?
Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigator at (203) 737-4777.

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

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Contact for Future Studies

We ask for your permission to contact you for participation in future studies that our group may conduct. We may use your telephone number, email address or mailing address to contact you.

I agree to be contacted for future studies I may qualify for: (initial your choice)

_____Yes _____No

Authorization and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

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