IRB Protocol#: 2000028252

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COMPOUND AUTHORIZATION AND CONSENT/PARENTAL PERMISSION FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY SCHOOL OF MEDICINE
YALE-NEW HAVEN HOSPITAL
YALE-NEW HAVEN HOSPITAL: SAINT RAPHAEL CAMPUS

Study Title: A randomized control trial to determine weight gain benefits of caloric supplementation for NAS infants

Principal Investigator (the person who is responsible for this research):

Matthew Grossman, MD; Mailing address:
Pediatric Critical Care Medicine
PO Box 208064 New Haven, CT 06520-8064
Phone Number: **203-785-4651**
24-Hour Phone Number: **N/A**

Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to examine the impact of caloric intake on weight management of infants with Neonatal Abstinence Syndrome (NAS).
- Study procedures will include: use of standard-calorie or high-calorie formula, twice daily infant weight checks, logging of weight, feeding, and other habit data for 14 days post enrollment with brief daily check in's with study staff. Updated data would be collected from the infant's pediatrician at regularly scheduled well child visits after the 14 days of active participation.
- After hospital discharge, the study team will call you to check in and gather data once daily through the end of the 14-day study intervention.
- No visits outside of the infant's regularly scheduled well child visits are required.
- There are some risks/inconveniences of participating in this study. These include the risk of excessive weight gain or weight loss, formula intolerance, and the inconvenience of twice daily weighing and logging of infant habits.
- The study may have no benefits to you. This study may or may not help with the weight management of your infant. Broadly this study has the potential to guide feeding management in infants born with NAS, and subsequently lead to better management of weight loss and reduced hospital length of stay in this population.
- There are other choices available to you outside of this research. If you choose not to participate in the study, your infant will still receive the high-quality care to manage their NAS which may or may not include a higher calorie diet.
- 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.
- At the end of the study, we will inform you and your baby's pediatrician as to what diet your infant was assigned to. If interested, you may continue to purchase the commercially available formula provided in the study. If cost is an issue, you may qualify for assistance through the Women, Infants, and Children (WIC) program. After the conclusion of the 14-day period, we recommend you look to your child's pediatrician for guidance on feeding. We will

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gather your infant's weight through their first birthday, but you do not need to continue the study diet beyond the 14-day period.

- 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.

Why is this study being offered to me and my infant?

We are asking you and your infant to take part in a research study because you are between the ages of 18-45, pregnant/or recently post partum, and currently receiving methadone/buprenorphine from a licensed treatment facility. Your baby is likely to experience some symptoms associated with Neonatal Abstinence Syndrome (NAS) and this study may help them regulate their weight gain in the first two weeks of life. We are looking for roughly 112 participants to be part of this research study.

Who is paying for the study?

The Department of Pediatrics at Yale New Haven Hospital will be paying for this study.

Who is providing other support for the study?

The Investigational Drug Service at Yale New Haven Hospital is also providing support.

What is the study about?

The purpose of this study is to evaluate the impact of standard calorie vs high calorie diet regiments on weight gain in infants born with NAS.

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:

Participation in this study will focus on the caloric intake of your infant. You will be free to decide on your own whether you want to use formula and/or breastfeed, and if so, how much. If you choose to feed your infant formula, we will provide you with a 14-day supply of either standard- or high-calorie formula upon hospital discharge be given to your infant. If you choose to breastfeed, we will provide you with formula powder to mix as infant formula or to fortify pumped breastmilk for when your infant is bottle feeding.

We will weigh the infant twice daily in the hospital and will also provide you with a loaned scale to take home with you to weigh your infant daily up to 14-days old. Nurses will work with you while you are in the hospital to practice logging information about your baby. Once you are home, you will also be asked to keep track of your infant's feedings, stools, and weights daily up until your infant is 14 days old. For each feed, you will include the time of the feed, feeding method (breastmilk or formula), volume of the feed (oz), and any observations (e.g., spit-up with feeds, problems latching, etc.). You will also record time of dirty diapers. We will ask you to record your infant's weight twice daily. The scale is to be returned to the study team following the conclusion of the 14-day period. Your infant's weights and lengths for the first year of life beyond this 14-day period will be collected through your infant's pediatrician and your regularly scheduled well child visits.

What are the risks and discomforts of participating?

Participation in the study involves randomization to a standard-calorie or high-calorie diet. This is a decision often made by the attending physician but will be assigned through randomization in this study. There is not currently a standard of care for caloric-density of feeds for infants with NAS (both 20 kcal/oz and 24 kcal/oz are prescribed) and there is currently variability based on the provider's assessment. You will still be able to make independent decisions about breastfeeding throughout the study. Though uncommon, there are potential risks associated with this study, including, but not limited to: increased weight gain or loss and/or formula intolerance. The study team will be closely tracking your infant's weight through daily check-ins with you and will stop the study in the unlikely case of an adverse event. The study may also involve risks to the infant that are currently unforeseeable. The study team will guide you through the next steps and determine whether or not to continue or adjust your assigned formula. If you are recommended to adjust the formula for your baby, your baby will be withdrawn from the study and we will not collect any further data on them.

How will I know about new risks or important information about the study?
We will tell you if we learn any new information that could change your mind about taking part in this study.

How can the study possibly benefit me?
The study may result in successful weight management of your infant. You will also be provided with a loaned scale to use for the infant's first 14 days to track weight changes over this period. You will also have a member of the study team checking in on you and your infant daily until your infant is 14 days old.

How can the study possibly benefit other people?

The benefits to science and other people may include a better understanding **of feeding protocols in infants born with NAS, and subsequently lead to better management of weight loss and reduced hospital length of stay in this population.**

Are there any costs to participation?

If you take part in this study, you will not have to pay for any formula or breastmilk fortification for the first fourteen days, supplies, or study procedures, that are provided for this research only. You or your health insurance must pay for services, supplies, procedures, and care that are part of your routine medical care. You will be responsible for any co-payments required by your insurance.

Will I be paid for participation?

You will receive a $5 gift card for participating in this study. 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?

Instead of participating in this study, you have some other choices.
You could:

- Get treatment without being in a study. **Your infant will still be treated for any potential weight loss or other symptoms related to NAS. Their physician may or may not decide to include a high-calorie diet regimen as a part of the treatment plan.**
- Take part in another 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 we learn that you are hurting a child or an older person.

When we publish the results of the research or talk about it in conferences, we will not use your or your infant's name, DOB, or any other identifying information. All personal health identifiers and confidential information will be stored on an encrypted, password-protected laptop in a secure Box. All data that is collected under you or your infant's name will be de-identified and connected to a random series of numbers that cannot be traced back to you. All HIPAA identifiers will be deleted upon conclusion of the study.

Identifiers will be separated from the identifiable private information. After removal, the information could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject.

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.

We will be collecting information about you and your health and well as your child and your child's health. The specific information that we will collect, use, and share includes:

- Research study records including phone calls and study visits
- Medical and laboratory records of only those services provided in connection with this study.
- The entire research record and any related medical records for mother and infant held by Yale New Haven Hospital created from: August 2020 to December 2021.
- Infant weight measurements through first year of life including measurements obtained by the infant's pediatrician at well child visits.

By signing this consent form, you are giving permission for us to receive weight and length information from your child's pediatrician through your child's first birthday.

How will you use and share my information?

We will use your information to conduct the study described in this consent form. Information collected during the study will be used to determine best practices for feeding methods in NAS infants. If shared, your information will only be shared in aggregate form without personal identifying 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
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- The U.S. Food and Drug Administration (FDA)
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- 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.
- Principal Investigator of the study
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team
- Independent data consultant and others authorized to monitor the conduct of the Study

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.

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.

However, this is a double-blinded treatment study and if you sign this permission form, you will not be allowed to look at or copy your study related information until after the research is completed.

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 ***Matthew Grossman, MD at Pediatric Critical Care Medicine PO Box 208064*** at the Yale University, New Haven, CT 06520-8046.

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 ensure 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 or your infant are injured while on study, seek treatment and contact the study doctor 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/your infant are injured as a result of 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. You do not give up any of your legal rights by signing this form.

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.

We would still treat your infant with standard therapy or, at your request, refer you and your infant to a clinic or doctor who can offer this treatment. Not 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.

The researchers may withdraw you from participating in the research if necessary. Your infant will be withdrawn from the study if your infant is:
(1) still losing weight by the 10-day timepoint
(2) loses >12% of his or her birth weight
(3) gains an average of >75 g per day over a 10-day interval

What will happen with my data if I stop participating?

If you stop participating in the study, we will use the data obtained (i.e., infant weight measurements, reported adverse events) up until the date of withdrawal. No further data would be collected. Additionally, if the study is stopped early for your infant by choice or because of an adverse event, no further data will be collected. The study team will contact you about collecting the loaned scale. You are welcome to keep your daily log and the remining formula.

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, Matthew Grossman, MD, at **203-785-4651.**

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.

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.

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 Name (Mother)	Participant Signature (Mother)	Date
Participant Name (Infant)	Parent Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

Complete if the participant is not fluent in English and an interpreter was used to obtain consent. Participants who do not read or understand English must not sign this full consent form, but instead sign the short form translated into their native language. This form should be signed by the investigator and interpreter only. If the interpreter is affiliated with the study team, the signature of an impartial witness is also required.

Print name of interpreter: _____

Signature of interpreter: _____ Date: _____

An oral translation of this document was administered to the participant in _____ (state language) by an individual proficient in English and _____ (state language).

Print name of impartial witness: _____

Signature of impartial witness: _____Date: _____

See the attached short form for documentation.