Restoring Emotional Needs with Exogenous ketones for Women (RENEW)
The Ohio State University
IRB Approval April 27, 2026
IRB# 2024H0455

The Ohio State University Consent to Participate in Research

Study Title:	**Restoring Emotional Needs with Exogenous ketones for Women (RENEW)**
Principal Investigator:	**Madison Kackley, PhD; Teryn Bedell, RD, Jeff Volek, RD, PhD**
Sponsor:	BHB Therapeutics/Juvanescence

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study

The following is a short summary to help you decide whether or not to take part in this study. More detailed information is provided later in this form.

You are being invited to take part in a research study to find out whether a 16-week lifestyle program that includes structured exercise, group behavioral support, and nutrition guidance, with or without a ketone supplement, can help improve mood and well-being in women aged 18–45 who are experiencing postpartum depression (PPD). If you choose to participate, you will be randomly assigned to one of two groups. You will attend weekly virtual exercise and group meetings, complete home and lab-based assessments, and take either a ketone supplement (Qitone™) or a placebo drink twice daily. This study will help researchers learn how these approaches affect mood, physical health, and recovery after childbirth. Possible risks include mild muscle soreness, stomach discomfort, or brief lightheadedness from blood draws. Your total participation will last about 18 weeks, and you will receive compensation for your time and travel.

1. Why is this study being done?

After giving birth, you may notice many physical, emotional, and social changes that can affect your mental health. Some women develop postpartum depression (PPD), which can cause persistent sadness, low energy, difficulty sleeping, loss of interest or pleasure in daily activities, and feelings of guilt or hopelessness. PPD can also affect your ability to bond with your baby and impact your overall family well-being.

This study, called RENEW (Restoring Emotional Needs with Exogenous Ketones for Women), is designed to see if a supportive lifestyle program can help you recover more effectively from PPD. The program combines regular exercise, healthy nutrition guidance, and group-based behavioral support, such as stress management and coping strategies. Research shows that exercise and behavioral interventions can improve mood, increase energy, reduce depressive symptoms, and provide social support by connecting you with other mothers who share similar experiences.

In addition to the lifestyle program, the study will also explore whether a supplement called exogenous ketones can further support your mood and mental clarity. Exogenous ketones increase levels of beta-hydroxybutyrate (BHB), a naturally occurring substance that may support brain energy and reduce inflammation. Early studies suggest higher BHB levels may be linked to fewer symptoms of depression, though this is still being researched.

By participating in this study, you will follow the lifestyle program, attend group sessions, and, if assigned, consume a ketone or placebo supplement daily. The study will monitor your mood, energy, cognition, and physical health over 16 weeks, while you continue your regular care with your healthcare providers. The goal is to help you feel more supported, improve your mental health, and enhance your overall well-being during the postpartum period.

2. How many people will take part in this study?

Up to forty (40) participants will take part in the study.

3. What will happen if I take part in this study?

This study is about 17 weeks long (1-week baseline period plus a 16-week intervention period). It includes 5 in-person study appointments. Of the 5 appointments, you will complete the first appointment at baseline (BL), one at Week-4, one at week-8, one at week-12, and one at week-16. This will be in addition to your regularly scheduled appointments with your psychiatric treatment provider. You will also be asked to complete online questionnaires via RedCap or Qualtrics every 2 weeks. **Table 1** describes the assessments at each study appointment. Additional details of the assessments for each appointment are described starting on Page 3. Baseline appointments can be shortened, if

necessary, to fit your schedule. For example, appointment 3 may be broken up into two separate sessions if it fits your schedule better.

RENEW Study Design

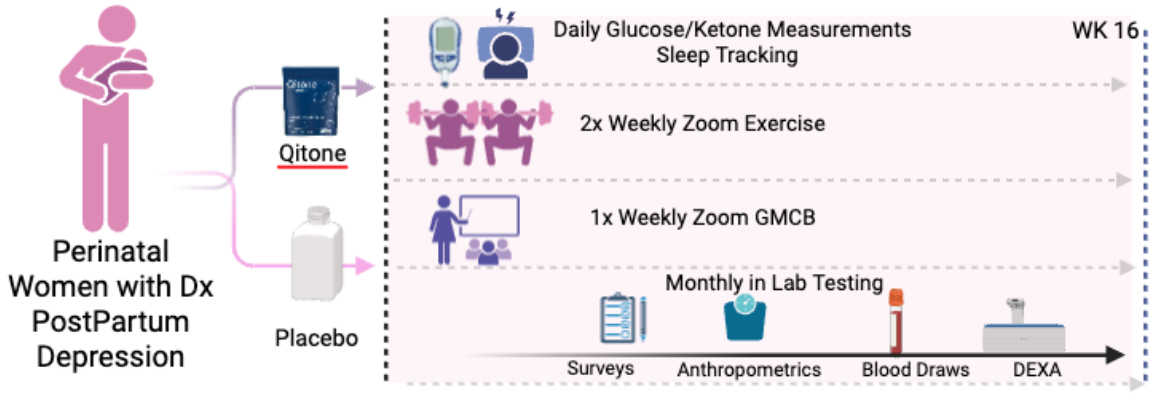


Figure 1: RENEW Study Design

Table 1: Scheduled study visits.

Study Procedures-

Study Method	**Screening**	**Daily**	**1x Week**	**2x Week**	**Monthly Lab testing**
Visit to Study Center	X				X
Informed consent	X				
Medical intake questionnaire, diet assessment, anthropometrics[1]	X				
Mental Health Battery	X				
Cognitive Testing	X				X (Wk 8 and 16)
Anthropometrics	X				X
Glucose and Ketone fingerstick Measurements		X			
Basal Body Temperature [3]		X			
Sleep tracking		X			
Take ketone or supplement		X			
Zoom GMCB			X		
Zoom exercise				X	
DEXA					X
Survey/Side effects					X
Hydration Status					X

Study Method	Screening	Daily	1x Week	2x Week	Monthly Lab testing
Venous Blood draw					X
Blood Pressure					X
Pregnancy Test					X
Follow-up Interview (Week 16 only)					

Ten hours before each visit you will be asked to refrain from eating food or drinking (beside water). Furthermore, you will refrain from consuming tetrahydrocannabinol (THC) products (cannabis products), alcohol, or performing extraneous exercise.

Eligibility Screening: After I have read through this form with you and you decide to consent to this study, you will be interviewed about your mental health history and current symptoms. You will also complete self-report questionnaires about your current dietary habits, mood, mental health, and typical behaviors. These measures will be used to determine your eligibility for the study. If any of these measures indicate that you are ineligible or it is unsafe for you to participate, then you will not be able to be in the study. If you meet the eligibility, you will be asked to participate in the following study components:

Assessments

Lab Visits

Clinical Interview/Behavioral Assessment (baseline, week 8 and week 16): At these appointments (estimated duration of 2 - 3 hours, with scheduled breaks), you will be asked a variety of questions about your mental and physical health, sleep, and fitness habits. You will also be asked to fill out an online survey to assess depressive symptoms via an internet-based survey and questionnaire administration program (REDCap / Qualtrics) every two weeks. Additionally, you may also be asked to fill out demographic, mood, health, or behavioral questionnaires.

Body Composition Assessment (baseline and week-16): You will also be asked to complete a dual-energy x-ray absorptiometry (DXA) scan. You will lie still on a table while the DXA machine takes pictures of your body (approximately 4-5 min) and gives us results of body fat and muscle mass. Female participants must complete a pregnancy test (urine HCG) prior to the DXA scan. This research study involves exposure to radiation from a DEXA EXPERT spine, femur or whole-body scan. This radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation that you will receive in this study is about 0.78 mSv or 78 mrem and is approximately equivalent to a uniform whole-body exposure of 95 days of exposure to natural background radiation. This use involves minimal risk and is necessary to obtain the research information desired.

Blood Draw (baseline, week-4, week-8, week-12 and week-16): A blood draw will be performed by a trained individual. During this procedure, the skin overlying the large veins of the forearm will be carefully cleaned with alcohol. A needle will then be inserted into the vein and approximately 40 ml (2.7 Tablespoons) of blood drawn into multiple tubes. The study team will process the blood for determination of various health markers.

At Home

Group-Mediated Cognitive Behavioral (GMCB) Counseling: Participants will engage in one weekly virtual Group-Mediated Cognitive Behavioral (GMCB) session (30–45 minutes per session) delivered via a HIPAA-compliant videoconferencing platform. The GMCB framework is an evidence-based behavioral counseling model designed to support sustained health behavior change through structured group support, self-regulation strategies, and cognitive skill development.

Sessions will focus on:

- Goal setting and self-monitoring
- Cognitive reframing and problem-solving
- Stress management and coping strategies
- Building social support and accountability
- Enhancing adherence to physical activity and nutrition-related behaviors

The GMCB sessions are educational and supportive in nature and do not constitute psychotherapy. Sessions will be led by trained study personnel following a standardized curriculum and will progress through adoption, transition, and maintenance phases across the 16-week intervention period.

Supervised Exercise Intervention: Participants will complete two supervised virtual exercise sessions per week (approximately 30 minutes per session) delivered via secure videoconferencing. Exercise sessions will include a combination of resistance-based and interval-style aerobic activities, designed specifically for postpartum women and aligned with ACSM safety guidelines.

Exercise intensity will be individualized using ratings of perceived exertion (RPE 0–10), with modifications provided as needed based on postpartum status, fitness level, and participant feedback. Sessions are intended to promote physical activity engagement, metabolic health, and psychological well-being and are not designed to exceed light-to-moderate intensity.

Attendance, perceived exertion, and tolerability will be monitored as measures of adherence and safety. Participants may pause or discontinue exercise at any time.

Finger Sticks (daily): Throughout the duration of the dietary intervention, you will be asked to perform finger-stick testing each morning, 1 hour after consuming your prescribed drink to measure your blood glucose and ketone levels via a drop of blood. This drop of blood will provide us with the information we need to adjust your diet so that you maintain a specific level of ketones in your blood. You will be provided with the glucose/ketone meter, and we will teach you how to use it.

Sleep/Activity Monitor (daily)*:* A tracker (Ultrahuman ring) will be worn on your index finger to monitor your sleep and activity throughout the study.

Study Product Consumption: You will receive your study product and instructions on how and when to take it. You will take the study product every day, approximately 5 minutes after your first and last meal (week 3 onward). We will give you a cup to measure your study product.

Daily Study Beverage Log: You will be given a log to record that you have taken the study beverage each day. For the first four weeks, the log also includes questions to record if you had any side effects of the study beverages.

Tolerability Assessment: Every 2 weeks, you will speak with study staff on the phone. During the call, study staff will ask a series of questions regarding the presence and severity of symptoms over the 2-week period.

Diet Recall: You will be asked to recall your food consumption for a 24-hour period using a paper log for 1 day prior to the baseline visit and for 1 day during the last week of the study.

Study Product Distribution: You will be mailed enough study products for the fourth month of the study.

Analysis

All the blood we collect from you will be kept in a cold storage freezer in our biochemistry lab. Your samples will be labeled with your subject identifier and not your name to maintain confidentiality. We will be measuring several markers in your blood related to metabolism and cardiometabolic response. However, since we will be storing your blood for up to five years, we may think of other markers to measure that we did not think of prior to the start of this study. Any future analysis that we may conduct will be related to this current study only and will not be used for any other research study. You have the right to decline the use of your samples for any potential future analysis. Below are two check boxes indicating that you either will allow us or will not allow us to use your blood to measure future markers. If you select not to allow us to use your blood for future tests, then any leftover samples will be destroyed. Please select an option below and sign your name with today's date. The extra signature indicates that you have thought about, read and understand this option. Please keep in mind that the selection of either option will have no impact or penalty during your participation in the study, and you will not lose any benefits to which you are otherwise entitled.

____ **Yes**, I give permission to use my blood samples for any future analysis.

____ **No**, I do not give permission to use my blood samples for any future analysis.

Participant Signature: _____

Date: _____

4. How long will I be in the study?

Your participation in this study will last for a total of 17 weeks, split into one week of baseline testing and 16 weeks of dietary intervention. The Baseline (BL) visit will consist of 1-2 appointments, depending on your availability. Week-4, week-8, week-12, and week-16 of the intervention consist of 1-2 appointments each. We anticipate that it will take approximately 32 hours to complete all appointments for this study, 28 of which will be completed virtually. Refer to the table below for an exact breakdown of the duration of study activities.

Activity	**Duration (hours)**	**Times per Participant**	**Total Time (hours)**
Baseline Testing (In-Lab)	1	1-2	1
Monthly In-Lab Testing	0.75	4 (up to 8)	3
Virtual Exercise Classes	1	16	16
GMCB	0.75	16	12 **32 hours total**

5. Can I stop being in the study?

You may voluntarily withdraw from this study at any point. Please be aware that the study personnel may terminate your participation depending on your ability to take part in the study activities, such as an inability to complete portions of the assessment or if staff consider it to be unsafe for you to participate. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

Travel: Travel to The Ohio State University for the assessment appointments may be inconvenient.

Surveys: Surveys administered in this study are designed to evaluate psychological aspects of mood, satiety/hunger, which may make you uncomfortable. The surveys have potential to cause you to feel anxiety, stress, depressive feelings, etc. You can skip any question(s) that make you uncomfortable. Research key personnel will help to provide contact information for resources such as the student health center, medical center, or emergency department if necessary to aid with intense psychological distress induced by surveys.

Exercise Sessions: Participation in the virtual exercise classes may pose physical risks, including temporary muscle soreness, fatigue, or discomfort associated with gentle to moderate activity. There is also a possibility of aggravating pre-existing musculoskeletal

issues or sustaining minor strain if exercises are performed incorrectly. Because classes are completed at home, there is additional risk related to the surrounding environment. This includes loss of balance or tripping if the exercise space is not clear. Symptoms such as dizziness, shortness of breath, or light-headedness may occur with exertion. These risks are minimized by instructor guidance, verbal cues, multiple exercise modifications, and clear recommendations to create a safe space for movement. Participants are encouraged to work at their own pace and may stop exercising at any time.

GMCB Sessions: Participation in the group-based motivational counseling (GMCB) sessions may pose emotional risks. These sessions involve guided discussions about postpartum experiences, emotional health, and topics related to postpartum depression. Participants may feel discomfort, sadness, or distress when discussing sensitive topics or hearing others' experiences. There is also an inherent privacy risk, as personal information shared by participants cannot be fully controlled or guaranteed to remain confidential despite group guidelines. These risks are minimized by the presence of a trained facilitator, clear expectations regarding confidentiality, the option to refrain from sharing, and the ability to leave the session at any time.

Body Composition-DXA: You will be exposed to a very small amount of radiation by the scanner used to measure your body composition. Exposure to any amount of X-ray radiation, no matter how low, may cause abnormal changes in cells. However, the body continuously repairs these changes, and the amount of radiation is very low in this study. DXA includes exposure to radiation similar to a flight from New York to Los Angeles or 125 times less than the radiation associated with a standard chest x-ray; any exposure to radiation may elevate cancer risk. The extra lifetime risk of dying of a fatal cancer due to the radiation exposure from this research may range from about one in 500,000 to about one in 200,000. At such low radiation exposures, scientists disagree about the amount of risk. These estimates are very uncertain, and there may be no extra risk at all. You will only be asked to complete the DXA assessment two times, which will minimize risks.

Study Product: All nutritional products carry a risk of side effects. Similar products have been tested in younger adults and we expect similar side effects in safety and tolerability. Side effects can range from mild to severe. If you experience moderate or severe side effects, notify the study staff as soon as possible. Please record them in the Study Beverage Log and keep from driving or operating heavy machinery if you feel unwell.
Below is a list of the most common general effects of taking ketones:

- Gas/flatulence
- Nausea (Sick to your stomach)
- Vomiting
- Abdominal cramping
- Stomach rumbling
- Burping
- Reflux (heartburn)
- Diarrhea

- Headache
- Dizziness or lightheadedness

If you experience side effects for several days when we increase the amount of study product you take, we might reduce the daily serving back to a level that didn't cause side effects. You must let a study investigator or study staff know about any and all side effects that you have. If you are not honest about your side effects, you may harm yourself by staying in this study.

Fasting:
You may experience the following side effects from fasting before each study visit such as:

- Nausea (Sick to your stomach)
- Dizziness or lightheadedness
- Headache

Fatigue (Low energy)

Finger-stick Testing: The finger stick may cause a slight immediate discomfort at the specific stick site. Under normal conditions, there are minimal risks to you when performing finger-sticks that include: bruising; light-headedness or dizziness due to fear of needles; and infection.

Blood Draws: Blood draws may cause discomfort at the skin puncture site and a small bruise may develop that may persist for several weeks. There is also a small possibility of an infection. Every precaution to avoid infection will be taken including the use of sterile disposable needles and gauze and the practice of aseptic (sterile) techniques during the blood draw.

Breach of Confidentiality: During pre-study talk with the research team (via email or phone), your name was recorded and there is the minimal risk that a breach of confidentiality could occur. To decrease the minimal risk of breach of data confidentiality, we strictly adhere to proper record keeping and safekeeping practices.

Focus Groups: While we ask other group participants to keep the discussion in the group confidential, we cannot guarantee this. Please keep this in mind when choosing what to share in the group setting.

7. What benefits can I expect from being in the study?

At the end of the study, we will provide you with your data about how you responded to the intervention. This feedback is not diagnostic in any way. At the end of the study and after we have completed all the analysis, you will also receive your own results back and you will be able to see if the diet has led to any improvements in your health, mood, or performance.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. Will my study-related information be kept confidential?

For all the data collected over the course of the study, (i.e., records, biological samples and questionnaires) a unique subject identifier (i.e., a code) will be assigned and used instead of your name. This identifier, which links your name to your data, will only be available to research personnel. Any records that contain your name and identifier together will either be stored in a storage room in a locked file cabinet or protected on a computer via password protection on the individual digital file and password protection on the computer the file(s) are stored on. All other records that only contain the subject identifier will be kept in either a file cabinet in our locked file storage room or on a password protected computer. Your name will never be used in any presentation or publication resulting from this study. The records will be maintained until the data are published.

There may be circumstances where your information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law. We may have to release your information if a law requires us to do so, the Agency that is funding this study requests the information, or if the FDA tells us to release this information. For example, we may disclose medical information (confidentiality will be broken) in cases of medical necessity or take steps (including notifying authorities) to protect you or someone else from serious harm, including child or elder abuse, or if you are in immediate danger of harming yourself or others.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office records. Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information.

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 the website at any time.

You may also be asked to sign a separate Health Insurance Portability and Accountability Act (HIPAA) research authorization form if the study involves the use of your protected health information.

10. Will my de-identified information and bio-specimens be used or shared for future research?

Yes, they may be used or shared with other researchers without your additional informed consent.

11. What are the costs of taking part in this study?

There are no costs to participate in the study. You may need to pay for parking if you do not have an Ohio State University parking pass, but we have temporary passes that we may be able to provide you.

12. Will I be paid for taking part in this study?

By law, payments to participants are considered taxable income. You are eligible to receive up to **$150** if you complete the entire study. Payment will be pro-rated by visit and will be in the form of electronic gift cards distributed in two installments to encourage continued participation and completion of study procedures.

- $75 will be provided after completion of the midpoint (Week 8) assessments.
- $75 will be provided after completion of the final (Week 16) assessments.

13. What happens if I am injured because I took part in this study?

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

14. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

15. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact **Dr. Madison Kackley via email kackley.19@osu.edu. 305 Anne and John Glenn Avenue, Room A052.**

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact Dr. Madison Kackley via email kackley.19@osu.edu.

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form**.**

Printed name of participant	**Signature of participant**
	AM/PM
	Date and time
Printed name of person authorized to consent for participant (when applicable)	**Signature of person authorized to consent for participant (when applicable)**
	AM/PM
Relationship to the participant	**Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	AM/PM
	Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness**
	AM/PM
	Date and time
Printed name of witness	**Signature of witness**
	AM/PM
	Date and time