8. FOLLOW-UP EVALUATIONS

8.1 Summary of Evaluations Preformed During the Month 1 Visit

Month 1 Visit (± 3 days)

- Clinic weight
- Resting BP
- Vital signs
- BMI calculation (CR group only)
- Waist circumference
- ECG
- Blood chemistry, hematology and urinalysis
- Concomitant medications
- Adverse events
- BDI

The Study Coordinator should contact the participant at least a week prior to the visit as a reminder to confirm the appointment.

This visit is primarily designed to check the safety of participants in the CR Intervention group. Clinic staff certified in obtaining these measurements will need to be available. A physician needs to review all safety measurements and confirm that there are no concerns with participants' safety. It is expected this visit will take approximately 2-3 hours. Participants must be fasting.

8.2 Preparations and Conduction of the Month 1 Visit

The order of these procedures and tests can vary however the fasting blood and urine samples should be obtained early so the participant can be given breakfast. Since the order of the procedures may vary, a checklist will be used to monitor their completion.

8.2.1 Month 1 Preparation

The following materials are needed to conduct this visit:

- Clinic scale
- Blood and Urine Collection Kits
- BP equipment
- ECG equipment
- BMI calculation (CR group only)
- Digital Oral Thermometer
- Medications Form
- BDI Questionnaire
- Gulick II Tape measure
- Breakfast Meal
- Participant's Event Diary for review

8.2.2 Month 1 Conduction

Study Coordinator

- Greet participant and verify they are fasting for at least 12 hours. If the participant is not fasting, the visit needs to be rescheduled or the participant can complete this visit but must return to the clinic within a few days for blood and urine collection.
- If not fasted, mark the checklist to indicate that blood and urine will be obtained at another visit in a few days, schedule this visit and move on to another part of the visit.
- Explain procedures for today's visit.
- Address any questions and/or concerns the participant might have concerning the study or today's visit
- Document on a progress note that questions were addressed.
- Have the participant empty their bladder in preparation for the clinic weight measurement.
- Once the weight and laboratory procedures are completed provide the participant with a breakfast.
- Perform BMI calculation from weight/height measurements
- Review the participant adverse event diary and current medications.
- Notify a physician when the safety and other required measurements have been completed so the participant can leave.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except for undergarments.
- Bring the participant to the clinic CALERIE scale and weigh the participant as described in MOP section 9.3.1.
- Record weights on source form as described in MOP section 9.3.1.
- Measure the waist circumference as described in MOP section 9.3.5.
- Measure the heart rate and blood pressure as described in MOP sections 9.2.3 and 9.2.4.
- Complete the remaining vital sign measurements (respiratory rate and oral temperature) as described in MOP section 9.2.5.
- Take the participant and participant’s binder to the phlebotomist

ECG Technician (may be certified study coordinator or in-patient staff)

- Record the ECG as directed in MOP section 9.12

Phlebotomist

- Have the Month 1 visit safety lab kit from LabCorp/Esoterix ready.
- Collect blood and urine safety samples, process, and label for safety lab as described in MOP Section 12.0.
- Notify staff that the participant is ready to continue the visit.
- Take the samples to the lab for processing.
- Local laboratory processes and labels the samples and ships these to the study safety laboratory. The certified phlebotomist oversees all procedures related to the safety samples and shipping these to the safety lab.

- Local laboratory will keep an inventory of the shipment to the safety lab.

Physician

- Review the vital signs, BMI (CR group only) and ECG. Confirm the safety laboratory tests have actually been drawn at this visit.
- Review the safety laboratory test results, when available, and confirm that there are no concerns with participant safety.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.

Measurement Technician

- Have participant complete the BDI. Score the BDI as described in MOP section 9.10.4, and notify the study physician, staff psychologist, and/or intervention leader if a problem exists.

Psychologist (if BDI score indicates a depression)

- Please refer to MOP section 24.4.

Study Coordinator

- Review the participant's binder and confirm that the participant has completed all procedures for this visit.
- Schedule the participant for the 3 month visit and explain it will be very much like today's visit.

Research Assistant

- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give the completed CRFs to the Study Manager to double check.
- Send approved CRFs to DCRI.

Study Manager

- Check all CRFs generated for Visit 1 and approve.

8.3 Summary of Evaluations Performed During the Month 3 Visit

Month 3 Follow-up Visit (± 7 days)

- Clinic weight
- Resting BP
- Vital signs
- BMI calculation (CR group only)
- Waist circumference
- ECG
- Blood chemistry, hematology and urinalysis
- Blood for archive
- Concomitant medications
- Adverse events
- BDI

The Study Coordinator should contact the participant at least a week prior to the visit to confirm the appointment.

The Month 3 visit is primarily designed to check the safety of participants in the Intervention group. Clinic staff certified in obtaining these measurements will need to be available for the visit. A physician needs to review all safety measurements and confirm that there are no concerns with participants' safety. It is expected that this visit will take approximately 2-3 hours. Participants must be fasting.

8.3.1 Preparations and Conduction of the Month 3 Visit

The order of these procedures and tests can vary however the fasting blood and urine samples should be obtained early so the participant can be given breakfast. Since the order of the procedures may vary, a checklist will be used to monitor their completion.

8.3.2 Month 3 Preparation

The following materials are needed to conduct the Month 3 safety visit:

- Clinic scale
- Blood and Urine Collection Kits **(*note- there will be extra blood samples taken at this visit for long term storage therefore there will be extra tubes and sample vials for the University of Vermont**).
- BP equipment
- ECG equipment
- Digital Oral Thermometer
- Medications Form
- BMI calculator (CR group only)
- BDI Questionnaire
- Gulick II Tape measure
- Breakfast Meal
- Participant's Event Diary for review
- Month Supply of Vitamin/Mineral and Calcium Supplements

8.3.3 Month 3 Conduction

Study Coordinator

- Greet participant and verify they are fasting for at least 12 hours. If the participant is not fasting, the visit needs to be rescheduled or the participant can complete this visit but must return to the clinic within a few days for blood and urine collection.
- If not fasted, mark the checklist to indicate that blood and urine will be obtained at another visit in a few days, schedule this visit and move on to another part of the visit.
- Address any questions and/or concerns the participant might have concerning the study or today's visit
- Document on a progress note that questions were addressed.
- Have the participant empty their bladder in preparation for the clinic weight measurement.
- Once the weight and laboratory procedures are completed provide the participant with a breakfast.
- Review the participant adverse event diary and current medications.
- Notify a physician when the safety and other required measurements have been completed so the participant can leave.
- Perform BMI calculation from weight/height measurements.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except for undergarments.
- Bring the participant to the clinic CALERIE scale and weigh the participant as described in MOP section 9.3.1.
- Record weights on source form as described in MOP section 9.3.1.
- Measure the waist circumference as described in MOP section 9.3.5.
- Measure the heart rate and blood pressure as described in MOP sections 9.2.3 and 9.2.4.
- Complete the remaining vital sign measurements (respiratory rate and oral temperature) as described in MOP section 9.2.5.
- Take the participant and participant’s binder to the phlebotomist

ECG Technician (may be certified study coordinator or in-patient staff)

- Record the ECG as directed in MOP section 9.12

Phlebotomist

- Have the Month 3 visit safety lab kit from LabCorp/Esoterix ready.
- Have the Month 3 visit kit from the University of Vermont laboratory for long term storage.
- Collect blood and urine safety samples, process, and label for safety lab as described in MOP Section 12.0.
- Collect blood for archive.
- Notify staff that the participant is ready to continue the visit.
- Take the samples to the lab for processing.

- Local laboratory processes and labels the samples and ships these to the study safety laboratory and the long term storage samples to Vermont as directed. The certified phlebotomist oversees all procedures related to the safety samples and shipping these to the safety lab.
- Local laboratory will keep an inventory of the shipments to each lab.

Physician

- Review the vital signs, BMI (CR group only) and ECG. Confirm the safety laboratory has actually been drawn at this visit.
- Review the safety laboratory test results, when available, and confirm that there are no concerns with participant safety.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.

Measurement Technician

- Have participant complete the BDI. Score the BDI as described in MOP section 9.10.4, and notify the study physician, staff psychologist, and/or intervention leader if a problem exists.

Psychologist (if BDI score indicates a depression)

- Please refer to MOP section 24.4.

Study Coordinator

- Review the participant's binder and confirm that the participant has completed all procedures for this visit.
- Provide the participant with new 3 month supply of vitamin/mineral and calcium supplements and perform pill count.
- Schedule the participant for the Month 6 visit and explain it will be a longer visit with an overnight stay.

Research Assistant

- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give the completed CRFs to the Study Manager to double check.
- Send approved CRFs to DCRI.

Study Manager

- Check all CRFs generated for the Month 3 visit and approve.

8.4 Summary of Evaluations Performed for the CR Group During the Month 6 Visit Period

Month 6 Follow-up Visit (± 14 days)

- **Month 6 Visit 1 (Day -7)**
  Clinic Weight
  Resting BP
  Waist Circumference
  Vital Signs
  BMI calculation
  ECG
  Safety Labs: Blood Chemistry, Hematology and Urinalysis
  Assessment of AE's and Medication Changes

- **Month 6 Visit 2 (Day 0)**
  Clinic Weight
  Urine Pregnancy Test (local lab)
  DLW Dose
  DLW Urine Samples
  DXA – Body Composition
  DXA - BMD/BMC
  QOL/Psychological Questionnaires:
    - Rand SF-36, BDI, Profile of Moods States, PSS, PSQI, Derogatis, Food Cravings, FCI-II, Eating Inventory, WEL, MAEDS, BSQ

  Body Acceptability Morph (BAM)
  IDED-IV (If Needed Based on BAM and MAEDS)
  6-day diet record – directions
  Weight Log and instructions
  Assessment of AE's and Medication Changes

- **Month 6 Visit 3 (Day 7)**
  Clinic Weight
  DLW Urine Samples (2)
  Home Weights (Collect)
  7-day PAR (CR group only)
  6-day food record review
  Assessment of AE's and Medication Changes

- **Month 6 Visit 4 (Day 13 – Inpatient)**
  Assessment of AE's and Medication Changes
  Standard Dinner followed by overnight fast
  Core Body Temperature – administer a capsule
  Overnight stay

- **Month 6 Visit 5 (Day 14 - Inpatient)**
  Urine Pregnancy Test
  Clinic Weight
  DLW Urine Samples (2)
  RMR (CR group only)

Markers of Bone Turnover
Blood for archive
DXA – Body Composition
Cognitive Function Measures
CANTAB
Home Weights (Collect)
7-day PAR (CR group only)
Core Body Temperature – complete the measurement
Assessment of AE's

The study coordinator should contact the participant at least one month in advance to schedule or confirm the Month 6 evaluations. Schedule all 5 visits at the same time in order to confirm the correct spacing for DLW visits.

8.4.1 Preparations and Conduction of the Month 6 Visits for the CR Group

The order of these procedures and tests can vary, however every effort should be made to keep all tests within the specified visit. Since the order of the visit may vary, a checklist will be used to monitor completion of these procedures and special notation will be made for items that must be done in a certain order. All staff members involved with the procedures must check off the appropriate box on the visit checklist that the procedure was completed. The study coordinator must verify that the checklist for that visit is complete at the end of each visit.

8.4.2 Month 6 Visit 1 Preparation (CR Group)

The following materials and equipment are needed to conduct Month 6 visit 1:

- Clinic Scale (Digital)
- ECG Equipment
- BP Equipment
- BMI Calculator (CR group only)
- Digital Oral Thermometer
- Gulick II Tape Measure
- Blood and Urine Collection Kits for safety labs
- Breakfast Meal
- Medications Form
- Participant's Adverse Event Diary
- Month Supply of Vitamin/Mineral and Calcium Supplements

8.4.3 Month 6 Visit 1 Conduction (CR Group)

Study Coordinator

- Greet the participant; confirm they are fasting for at least 12 hours (water is allowed). If not fasted, reschedule the visit.
- Explain procedures for today's visit and for the entire Month 6 testing period.
- Address any questions and/or concerns the participant might have concerning the study or the Month 6 testing process.

- Have the participant empty their bladder in preparation for the clinic weight measurement.
- Once the weight and laboratory procedures are completed provide the participant with a breakfast.
- Review and record adverse events.
- Perform BMI calculation from weight/height measurements.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except for undergarments.
- Bring the participant to the clinic CALERIE scale and weigh the participant as described in MOP section 9.3.1.
- Record weights on source form as described in MOP section 9.3.1.
- Measure the waist circumference as described in MOP section 9.3.5.
- Measure the heart rate and blood pressure as described in MOP sections 9.2.3 and 9.2.4.
- Complete the remaining vital sign measurements (respiratory rate and oral temperature) as described in MOP section 9.2.5.
- Take the participant and participant's binder to the phlebotomist.

ECG Technician (may be certified study coordinator or in-patient staff)

- Record the ECG as directed in MOP section 9.12.

Phlebotomist

- Have the Month 6 visit safety labs kit from LabCorp/Esoterix ready.
- Collect blood and urine safety samples, process, and label for safety lab as described in MOP Section 12.0.
- Notify staff that the participant is ready to continue the visit.
- Take the samples to the lab for processing.
- Local laboratory processes and labels the samples and ships these to the study safety laboratory. The certified phlebotomist oversees all procedures related to the safety samples and shipping these to the safety lab.
- Local laboratory keep inventory of shipment to the safety lab.

Study Coordinator

- Review the participant's binder and confirm that the participant has completed all procedures for this visit.
- Provide participant 3 month supply of vitamin/mineral supplement and perform pill count. Remind participant not to take vitamin/mineral supplement the same day prior to DXA testing.
- Confirm the Month 6 testing schedule.
- If the participant has not already been scheduled for the remaining visits, schedule the visits now.
- Provide the physician with the ECG for review.

Physician

- Review the vital signs, BMI, and ECG and confirm that there are no concerns with participant safety.

- If there are safety concerns requiring further action, present a study coordinator with the action plan.

Research Assistant
- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give the completed CRFs to the Study Manager to double check.

Study Manager
- Check all CRFs generated for Visit 1 and approve.

8.4.4 Month 6 Visit 2 Preparation (CR Group)

The following materials and equipment are needed to conduct 6-month visit 2:
- DLW Dose
- DLW Urine Collection Kits
- Urine Pregnancy Test (local)
- Clinic Scale (Digital)
- DXA Machine
- Snack/Meal
- QOL/Psychological Questionnaires
- BAM
- IDED-IV (if Needed based on BAM and MAEDS)
- Home Scale, Weight Measurement Instructions and Weight Logs
- 6-day food record
- Adverse Events Diary/Medications List
- Results of safety laboratory tests

8.4.5 Month 6 Visit 2 Conduction (CR Group)

Study Coordinator
- Greet the participant and explain procedures for today's visit.
- Review the participant's diary and medications with the participant for any reported events. Proactively inquire if they experience any health changes since their last visit.
- Check that the participant has not taken any vitamin/mineral supplements the same day, prior to DXA testing.
- Confirm the participant is not pregnant prior to DXA testing.
- Provide safety laboratory results from earlier visit upon receipt from the lab to the physician to review.

DLW Technician
- Perform DLW Day 0 procedures as described in MOP section 10.0.
- Take participant and their binder to the DXA technician.

DXA Technician

- Perform the required DXA, BMD and BMC measurements as described in MOP section 9.6.1.
- Notify staff that the participant is ready to continue the visit.

Clinic Staff

- Provide the participant with a gown and instruct them to remove all clothing except for undergarments.
- Obtain urine for pregnancy testing and send to lab for stat processing.
- Bring the participant to the clinic CALERIE scale and weigh the participant as described in MOP section 9.3.1.
- Record weights on source form as described in MOP section 9.3.1.
- Provide the snack/meal from the kitchen staff to the participant after DXA testing is complete.

Measurement Technician/Measurement Leader

- Have participant complete the BDI, Eating Disorder Questionnaire, QOL assessments and Psychological assessments. Score the questionnaires as described in MOP section 9.10, and notify the study physician and intervention leader if a problem exists.
- BDI, MAEDS, BAM are safety measures and the latter may require the IDED-IV afterwards.
- Alert psychologist if IDED-IV is needed.

Psychologist

- Conduct IDED-IV if needed

Dietitian

- Instruct participants on completion of the 6-day food record as described in MOP section 9.5.
- Provide food record to participant.
- Verify that participant is taking supplements and has discontinued the use of any supplements that were not provided by the study.
- Notify staff that the participant is ready to continue the visit.

Study Coordinator

- Remind participant to bring their diary at the next visit.
- Review participant binder and confirm that all procedures for this visit have been completed.
- Confirm date and time of the next Month 6 visit and remind the participant to bring their weight log to the clinic.

Physician

- Review laboratory test results and confirm that there are no concerns with participant safety.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.

Research Assistant

- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to study Manager to double check.

Study Manager

- Check all CRFs generated for Visit 2 and approve.

8.4.6 Month 6 Visit 3 Preparation (CR Group)

The following materials are needed to conduct the 6-month visit 3:

- Clinic Scale (Digital)
- DLW Urine Collection Kits
- 7-day PAR
- 6-day Food Record
- Weight Logs
- Adverse Events Diary/Medications List

8.4.7 Month 6 Visit 3 Conduction (CR Group)

Study Coordinator

- Greet the participant, and explain procedures for today's visit.
- Review the home weights log with the participant as described in MOP section 9.3.4.
- Review the participant's diary and medications with the participant for any reported events. Proactively inquire if they experienced any health changes since the last visit.
- Perform the Stanford 7-day PAR as described in MOP section 9.7.3.
- Take the participant and participant's binder to the DLW technician.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except for undergarments. Have the participant empty their bladder before weighing.
- Bring the participant to the clinic CALERIE scale and weigh the participant as described in MOP section 9.3.1.
- Record weights on source form as described in MOP section 9.3.1.

DLW Technician

- Perform DLW Day 7 procedures as described in MOP section 10.0.

Dietitian

- Collect the participant's 6-day food record.
- Verify and document on the food record that participant is taking supplements and has discontinued the use of any supplements that were not provided by the study.

- Review the record for completeness and prepare for submission to the reading center according to the steps described in MOP sections 17.0.

Study Coordinator

- Review participant binder and confirm that all procedures for this visit have been completed.
- Confirm date and time of the next Month 6 visit and remind the participant not to exercise within 24 hours of next appointment. Also remind to bring weight log and diary to the clinic at next visit.

Research Assistant

- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the Study Manager.

Study Manager

- Check all CRFs generated for Visit 3 and approve.

8.4.8 Month 6 Visit 4 Preparation (CR Group Inpatient Stay)

The following materials and equipment are needed to conduct Month 6 visit 4-5:

- Core Temp Capsule and Equipment
- Dinner
- Adverse Events Diary/Medications List

8.4.9 Month 6 Visit 4 Conduction (CR Group Inpatient Stay)

Inpatient Nursing Staff

- Admit participant to the inpatient unit by 4:00 pm
- Provide participant with the standard dinner prepared by the metabolic kitchen.
- Administer the core temperature capsule by 6:00 pm and document the time of administration. Oversee the attachment of the core temperature monitor for recording the core temperature over the next 24 hours. The monitor will be worn for a total of 26 hours after the capsule is swallowed, as an additional measure to obtain an accurate 24 hours core temperature recording. Please refer to MOP section 9.4.2 for further instructions.
- Remind the participant that he/she is required to fast overnight. Only water is allowed after dinner and water must be at room temperature.
- Remind participant to not take vitamin/mineral supplement the morning prior to DXA testing.

Core Body Temperature Measurement Technician

- Perform core body temperature measurement as described in MOP section 9.4.5.

8.4.10 Month 6 Visit 5 Preparation (CR Group Inpatient Stay)

The following materials and equipment are needed to conduct Month 6 visit 5:

- Clinic Scale (Digital)
- Urine Pregnancy Test (local lab)
- DLW Urine Collection Kits
- Core Temperature Equipment
- RMR Equipment
- 7-day PAR
- Weight Logs
- Blood Collection Kits for the outcome measurements
- Blood Kits for Archive
- Cognitive Function Measures
- CANTAB
- Meals
- DXA Equipment
- Participant's Event Diary

8.4.11 Month 6 Visit 5 Conduction (CR Group Inpatient Stay)

Inpatient Nursing Staff

- Wake the participant at 7:00 am and explain procedures for today's visit.
- Provide the participant with a gown and instruct them to remove all clothing except for undergarments.
- Obtain urine sample for pregnancy testing and have participant empty their bladder before weighing. Pregnancy test to be run stat in local lab to get results prior to DXA testing.
- Bring the participant to the clinic CALERIE scale and weigh the participant as described in MOP section 9.3.1.
- Record weights on source form as described in MOP section 9.3.1.
- Ask the participant to collect two separate DLW urine samples as directed in MOP section 10.0. Call the DLW Technician for pick-up after the collection of the 2 urine samples.
- Remind participant to not take vitamin/mineral supplements until after the completion of their DXA scan.
- Provide meals throughout the day as directed by the kitchen staff. **No meals should be served until the completion of the RMR, laboratory tests and DXA! All liquids must be served at room temperature during core temperature recording!**
- Take the core temperature monitor off the participant in 26 hours after the first signal was recorded as directed by the Core Body Temperature measurement technician.
- Provide overnight supervision for the participant.

Core Body Temperature Measurement Technician

- Verify that the participant is still wearing their core temperature monitor and inform the nursing staff when it is time for removal.
- Verify the core temperature monitor is recording and participant is following instructions for this procedure.

DLW Technician

- Perform DLW Day 14 procedures as described in MOP section 10.0.

RMR Technician

- Perform RMR measurement as described in MOP Section 9.4.1.
- Take the participant and participant's binder to the coordinator.

Study Coordinator

- Review the home weights log with the participant as described in MOP section 9.3.4.
- Review participant's diary and medications with the participant for any reported events. Proactively inquire if they experienced any health changes since the last visit.
- Check that the final DLW samples have been collected and the 24-hour urine collection is in progress.
- Perform the Stanford 7-day PAR as described in MOP section 9.7.3.
- Confirm the participant is not pregnant prior to DXA testing.
- Take the participant and participant's binder to the phlebotomist.

Phlebotomist

- Have the Month 6 visit outcomes kit from the University of Vermont lab ready.
- Collect blood for markers of bone turnover and blood samples for archival. Take these to the local laboratory for processing and labeling for the University of Vermont lab as described in MOP Section 11.0. This will include extra aliquots for long-term storage. (Samples that cannot be processed immediately must be stored under recommended conditions until processed – please refer to MOP section 11.0).
- Local laboratory - store samples under recommended conditions until they are shipped to the Vermont laboratory as described in MOP Section 11.0.
- Ship samples to the laboratory as described in MOP Section 11.0.
- Document the shipment.
- Notify staff that the participant is ready to continue the visit.

DXA Technician

- Perform the required DXA, BMD and BMC measurements as described in MOP section 9.6.1.
- Notify staff that the participant is ready to continue with the next part of their visit.

Measurement Staff

- Perform the CANTAB testing after meal.
- Prepare the participant for Cognitive Function testing and complete testing.

Study Coordinator

- Review participant binder and confirm that all procedures for this visit have been completed.

Research Assistant

- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the study manager to double check.

Study Manager

- Check all CRFs generated for the in-patient stay and approve.

This concludes the Month 6 testing period for the CR group. The participant's binder and chart should be reviewed for any missing or incomplete data and any remaining Month 6 CRF sections completed and sent to the CC.

8.5 Summary of Evaluations Performed for the Control Group During the Month 6 Visit Period

Month 6 Follow-up Visit (± 14 days)

- **Month 6 Visit 1 (Control Group Inpatient Stay)**
  Standard Dinner followed by overnight fast
  Core Body Temperature – administer a capsule
  Overnight stay

- **Month 6 Visit 2 (Control Group Inpatient Stay)**
  Clinic Weight
  Resting BP
  Waist Circumference
  Vital Signs
  ECG
  Blood Chemistry, Hematology and Urinalysis
  Blood for archive
  Markers of Bone Turnover
  QOL/Psychological Questionnaires:
    - Rand SF-36, BDI, Profile of Moods States, PSS, PSQI, Derogatis, Food Cravings, FCI-II, Eating Inventory, WEL, MAEDS, BSQ

  Body Acceptability Morph (BAM)
  IDED-IV if needed
  Cognitive bias testing
  CANTAB
  Assessment of AE's and Medication Changes
  Core Body Temperature – complete the measurement
  Assessment of AE's and Medication Changes

The study coordinator should contact the participant at least one month in advance to schedule or confirm the Month 6 evaluations. Schedule both visits at the same time.

8.5.1 Preparations and Conduction of the Month 6 Control Group Visits

The order of these procedures and tests can vary, however every effort should be made to keep all tests within the specified visit. Since the order of the visit may vary, a checklist will be used to monitor completion of these procedures and special notation will be made for items that must be done in a certain order. All staff members involved with the procedures must check off the appropriate box on the visit checklist that the procedure was completed. The study coordinator must verify that the checklist for that visit is complete at the end of each visit.

8.5.2 Month 6 Visit 1 Preparation (Control Group Inpatient Stay)

The following materials and equipment are needed to conduct 6-month visit 1:

- Core Temp Capsule and Equipment
- Dinner

8.5.3 Month 6 Visit 1 Conduction (Control Group Inpatient Stay)

Inpatient Nursing Staff

- Admit participant to the inpatient unit by 4:00 pm
- Provide participant with the standard dinner prepared by the metabolic kitchen.
- Administer the core temperature capsule by 6:00 pm and document the time of administration. Oversee the attachment of the core temperature monitor for recording the core temperature over the next 24 hours. The monitor will be worn for a total of 26 hours after the capsule is swallowed, as an additional measure to obtain an accurate 24 hours core temperature recording. Please refer to MOP section 9.4.2 for further instructions.
- Remind the participant that he/she is required to fast overnight. Only water is allowed after dinner. Liquids must be at room temperature after ingestion of the core temperature capsule.

Core Body Temperature Measurement Technician

- Perform core body temperature measurement as described in MOP section 9.4.2.

8.5.4 Month 6 Visit 2 Preparation (Control Group Inpatient Stay)

The following materials and equipment are needed to conduct 6-month visit 2:

- Clinic Scale (Digital)
- BAM
- IDED-IV if needed
- Cognitive bias testing
- CANTAB
- QOL questionnaires
- Psychological questionnaires
- ECG Equipment
- BP Equipment
- Digital Oral Thermometer
- Gulick II Tape Measure
- Blood and Urine Collection Kits for safety labs
- Medications Form
- Participant's Adverse Event Diary
- Core Temperature Equipment
- Meals
- Month Supply Vitamin/Mineral and Calcium Supplements

8.5.5 Month 6 Visit 2 Conduction

Inpatient Nursing Staff

- Wake the participant at 7:00am and explain procedures for today's visit.
- Provide the participant with a gown and instruct them to remove all clothing except for undergarments.

- Bring the participant to the clinic CALERIE scale and weigh the participant as described in MOP section 9.3.1.
- Record weights on source form as described in MOP section 9.3.1.
- Measure the waist circumference as described in MOP section 9.3.5.
- Measure the heart rate and blood pressure as described in MOP sections 9.2.3 and 9.2.4.
- Complete the remaining vital sign measurements (respiratory rate and oral temperature) as described in MOP section 9.2.5.
- Provide meals throughout the day as directed by the kitchen staff. **Liquids must be at room temperature.**
- Take the core temperature monitor off the participant in 26 hours after the first signal was recorded as directed by the Core Body Temperature Measurement technician.
- Discharge participant after completion of the visit procedures and core temperature recording.

Measurement Technician

- Have participant complete the BDI and all other questionnaires after the participant has eaten a meal. The BDI should be scored as described in MOP Section 9.10.4 and notify the study physician and intervention leader if a problem exists so a suicide assessment may be conducted.
- Score the MAEDS questionnaire.
- Perform the BAM testing.
- Note: If the scores on the BAM and or CANTAB require an IDED-IV, alert the staff psychologist so an IDED-IV can be administered.
- Perform the CANTAB testing after meal.
- Prepare the participant for Cognitive Function testing and complete testing.

Psychologist

- Conduct IDED-IV if needed

ECG Technician (may be certified study coordinator or in-patient staff)

- Record the ECG as directed in MOP section 9.12.

Core Body Temperature Measurement Technician

- Verify that the participant is still wearing their core temperature monitor and inform the nursing staff when it is time for removal.

Phlebotomist

- Have the Month 6 visit outcome and safety lab kits from LabCorp/Esoterix and from the University of Vermont ready.
- Collect blood and urine safety samples, process, and label for safety lab, collect blood for the Vermont laboratory as described in MOP Section 12.0.
- Notify staff that the participant is ready to continue the visit.
- Take all samples to the lab for processing.
- Local laboratory processes and labels the samples and ships these to the study safety laboratory and Vermont laboratory. The certified phlebotomist oversees all procedures related to the safety samples and shipping these to the safety lab.

- Local laboratory keep inventory of shipments to the safety and outcome labs.

Physician

- Review the vital signs and ECG and confirm that there are no concerns with participant safety.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.
- Review safety laboratory test results when received and confirm that there are no concerns with participant safety.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.

Study Coordinator

- Provide the Physician with the ECG for review.
- Review participant's diary and medications with the participant for any reported events. Proactively inquire if they experienced any health changes since the last visit.
- Provide participant 3 month supply of vitamin/mineral and calcium supplements and perform pill count.
- Review the participant's binder and confirm that the participant has completed all procedures for this visit.
- Provide the physician with the safety labs once received for review.

Research Assistant

- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the study manager to double check.

Study Manager

- Check all CRFs generated for the in-patient stay and approve.

This concludes the Month 6 testing period for the Control Group. The participant's binder and chart should be reviewed for any missing or incomplete data and any remaining 6-month CRF sections completed and sent to the CC.

8.6 Summary of Evaluations Preformed During the Month 9 Visit

Month 9 Visit (± 14 days)

Clinic weight
Resting BP
Vital signs
Waist circumference
ECG
Blood chemistry, hematology and urinalysis
Concomitant medications
Adverse events
BMI calculation (CR group only)
BDI

The study coordinator should contact the participant at least a week prior to the visit to confirm the appointment.

This visit is primarily designed to check the safety of participants in the Intervention group. Clinic staff certified in obtaining these measurements will need to be available. A physician must review all safety measurements and confirm that there are no concerns with participants' safety. It is expected this visit will take approximately 2-3 hours. Participants need to be fasting.

8.6.1 Preparations and Conduction of the Month 9 Visit

The order of these procedures and tests can vary however the fasting blood and urine samples should be obtained early so the participant can be given breakfast. Since the order of the procedures may vary, a checklist will be used to monitor their completion.

8.6.2 Month 9 Preparations

The following materials are needed to conduct this visit:

- Clinic scale
- Blood and Urine Collection Kits
- BP equipment
- ECG equipment
- Digital Oral Thermometer
- Medications Form
- BMI Calculator (CR group only)
- BDI Questionnaire
- Gulick II Tape measure
- Breakfast Meal
- Participant's Event Diary for review
- Month Supply Vitamin/Mineral and Calcium Supplements

8.6.3 Month 9 Conduction

Study Coordinator

- Greet participant and verify they are fasting for at least 12 hours. If the participant is not fasting, the visit needs to be rescheduled or the participant can complete this visit but must return to the clinic within a few days for blood and urine collection.
- If not fasted, mark the checklist to indicate that blood and urine will be obtained at another visit in a few days, schedule this visit and move on to another part of the visit.
- Address any questions and/or concerns the participant might have concerning the study or today's visit
- Document on a progress note that questions were addressed.
- Have the participant empty their bladder in preparation for the clinic weight measurement.
- Once the weight and laboratory procedures are completed provide the participant with a breakfast.
- Review the participant adverse event diary and current medications.
- Perform BMI calculation from weight/height measurements
- Notify a physician after the completion of the measurements and laboratory procedures have been completed so the participant can leave.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except for undergarments. Participant should empty bladder before weighing.
- Bring the participant to the clinic CALERIE scale and weigh the participant as described in MOP section 19.3.1.
- Record weights on source form as described in MOP section 9.3.1.
- Measure the waist circumference as described in MOP section 9.3.5.
- Measure the heart rate and blood pressure as described in MOP sections 9.2.3 and 9.2.4.
- Complete the remaining vital sign measurements (respiratory rate and oral temperature) as described in MOP section 9.2.5.
- Take the participant and participant's binder to the phlebotomist

ECG Technician (may be certified study coordinator or in-patient staff)

- Record the ECG as directed in MOP section 9.12

Phlebotomist

- Have the Month 9 visit safety lab kit from LabCorp/Esoterix ready.
- Collect blood and urine safety samples, process, and label for safety lab as described in MOP Section 12.0.
- Notify staff that the participant is ready to continue the visit.
- Take the samples to the lab for processing.
- Local laboratory processes and labels the samples and ships these to the study safety laboratory.
- The certified phlebotomist oversees all procedures related to the safety samples and shipping these to the safety lab.
- Local laboratory will keep an inventory of the shipment to the safety lab.

Physician

- Review the vital signs, BMI (CR group only) and ECG. Confirm the safety laboratory has actually been drawn at this visit.
- Review the safety laboratory test results, when available, and confirm that there are no concerns with participant safety.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.

Measurement Technician

- Have participant complete the BDI. Score the BDI as described in MOP section 9.10.4, and notify the study physician, staff psychologist, and/or intervention leader if a problem exists.

Psychologist (if BDI score indicates a depression)

- Please refer to MOP section 24.4.

Study Coordinator

- Review the participant's binder and confirm that the participant has completed all procedures for this visit.
- Provide 3 month supply of vitamin/mineral and calcium supplements and perform pill count.
- Schedule the participant for the Month 12 visit and explain it will be a longer visit with an overnight stay.

Research Assistant

- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give the completed CRFs to the Study Manager to double check.
- Send approved CRFs to DCRI.

Study Manager

- Check all CRFs generated for the Month 9 visit and approve.

8.7 Summary of Evaluations Performed for Both Groups During the Month 12 Visit Period

Month 12 Follow-Up (± 14 Days)

Month 12 Visit 1 (Day 0)

Urine Pregnancy Test (local lab)
Resting BP
Vital signs
Clinic weight
Waist Circumference
BMI Calculation (CR group only)
ECG
Safety Labs: Blood Chemistry, hematology, and urinalyses
DLW Dose
DLW Urines
Physical Exam
DXA
BMD/BMC
QOL/Psychological Questionnaires:

- Rand SF-36, BDI, Profile of Moods States, PSS, PSQI, Derogatis, Food Cravings, FCI-II, Eating Inventory, WEL, MAEDS, BSQ

Body Acceptability Morph (BAM)
IDED-IV (If needed based on BAM and MAEDS – may be moved to Month 12 Visit 2 if cannot be performed at this visit)
Cybex (Muscle Strength)
6-day Food Record - directions
Assessment of AE's and medication changes
Issue home scale with directions to control participants

Month 12 Visit 2 (Day 7)

Clinic Weight
DLW Day 7 Urines
Home Weights (collect)
7-day PAR
IDED-IV (if needed and not preformed at earlier Month 12 Visit)
6-day Food Record - review
Assessment of AE's and medication changes
$V0_2$ Max test

Month 12 Visit 3 (Day 13)

DTH test
Standard Dinner (High Carbohydrate Meal)
Core Body Temperature – administer a capsule
Assessment of AE's and medication changes
Overnight stay

Month 12 Visit 4 (Day 14)

Clinic Weight
DLW Urine

Home Weights (Collect)
7-day PAR
DTH 24 hour Reading
RMR
Core Body Temperature - complete the measurement
OGTT
Blood/Urine for Archive
Repeat Sex hormone – Females (1 hour after first sample)
Lab Work: Cardiovascular Risk Factors, insulin, C-peptide, sex hormones, bone markers, endocrine response and growth factors
Cognitive Function Measures
CANTAB
Overnight Stay
Assessment of AE's and medication changes

Month 12 Visit 5

Sex hormones – Females only
Muscle Biopsy (follow-up within 3 days to check that the site is healing)
Fat Biopsy
DTH 48 hour reading
Assessment of AE's and medication changes
Discharge

Phone Follow-Up for Biopsy Check

Progress Note for phone follow-up

The study coordinator should contact the participant at least 1 month in advance to schedule or confirm scheduling of the Month 12 evaluations. Schedule all 5 visits at the same time in order to confirm the correct spacing for DLW periods.

8.7.1 Preparation and Conduction of Month 12 Visits

In some cases, the order of these procedures and tests can vary, however every effort should be made to keep all tests within the specified test day. Since the order of the visit may vary, a checklist will be used to monitor completion of these procedures and special notation will be made for items that must be done in a certain order. All staff members involved with the procedures must check off the appropriate box on the visit checklist that the procedure was completed. The study coordinator must verify that the checklist for that visit is complete at the end of each visit.

8.7.2 Month 12 Visit 1 Preparation

The following materials are needed to conduct the Month 12 visit 1:

- Clinic Scale (Digital)
- BMI Calculator (CR group only)
- ECG Equipment
- BP Equipment
- Gulick II Tape Measure
- Digital Oral Thermometer

- Home Scales, Directions and Weight Logs
- Physical Exam Form
- Blood and Urine Collection Kits
- Urine Pregnancy Test (local lab)
- DLW Dose
- DLW Urine Collection Kits
- DXA Machine
- QOL/Psychological Questionnaires
- BAM
- IDED-IV (if needed based on BAM and MAEDS – can also be moved to Month 12 Visit 2 if needed)
- Muscle Strength and Endurance Equipment
- Food Record Instructions and Food Records
- Adverse Event and Concomitant Medication Forms
- Participant's Adverse Event Diary
- Month Supply Vitamin/Mineral and Calcium Supplements

8.7.3 Month 12 Visit 1 Conduction

Study Coordinator

- Greet the participant; confirm they are fasting for at least 12 hours (water is allowed). If not fasted, reschedule the visit.
- Explain procedures for today's visit and for the entire Month 12 testing period.
- Review the participant's diary and medications with the participant for any reported events. Proactively inquire if they experience any health changes since their last visit.
- Confirm the participant has not taken their vitamin/mineral supplements prior to the DXA scan.
- Confirm that urine pregnancy test is negative before taking participant and their binder to the DXA technician.
- Perform BMI calculation based on height/weight information.
- Once the participant has completed the fasting procedures for the visit (weight and blood work), then provide the participant with a meal as specified at the site.
- Provide safety laboratory results upon receipt from the lab to the physician to review.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except undergarments. Have participant, if female, provide urine sample for pregnancy testing and empty bladder before weighing. Have pregnancy test run stat by local lab.
- Bring the participant to the CALERIE scale and have the participant weigh following the directions described in MOP section 9.3.1.
- Record weights on source document as directed in MOP section 9.3.1.
- Prepare patient for resting ECG and notify ECG technician to record ECG.
- Complete the waist circumference measurements as directed in MOP section 9.3.5.

- Prepare the participant for and perform resting heart rate and blood pressure measurements as described in section 9.2.3 and 9.2.4 of the MOP.
- Complete the remaining vital sign measurements (respiratory rate and oral temperature) as directed in MOP section 9.2.5.
- Bring the participant and the participant's binder to the phlebotomist for required blood work.
- Prepare participant for the physical exam.
- Assess all adverse events and concomitant medication changes and record on appropriate forms. See MOP sections 22.0 for further instructions.
- Confirm a negative urine pregnancy test for all applicable participants and send participant to have DXA.
- Send the participant to the muscle strength and endurance testing area.

ECG Technician (may be certified study coordinator or in-patient staff)

- Record the ECG as directed in MOP section 9.12

Phlebotomist

- Have the Month 12 visit safety labs kit from LabCorp/Esoterix ready.
- Collect blood and urine safety samples, process and label for safety lab as directed in MOP section 12.0.
- Notify staff that the participant is ready to continue with the next parts of the visit.
- Take the samples to the lab for further processing.
- Local laboratory processes and labels the samples and ships these to the study safety laboratory. The certified phlebotomist oversees all procedures related to the safety samples and shipping these to the safety lab.
- Local laboratory keep inventory of shipment to the safety lab.
- Document that samples were picked up.

DLW Technician

- Perform DLW Day 0 procedures as described in MOP section 10.0.

DXA Technician

- Perform the required DXA, BMD and BMC measurements as described in MOP section 9.6.1.
- Notify staff that the participant is ready to continue with the visit.

Physician

- Review vital signs, adverse events, concomitant medications and ECG, and confirm that there are no concerns with participant safety. Confirm the safety laboratory has actually been drawn at this visit.
- Perform a physical examination to confirm continuing eligibility of the participant.
- Document physical exam results on the physical exam form provided by the study coordinator.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.
- Notify staff that the participant is ready to continue the visit.

Measurement Technician

- Provide Quality of Life and Psychological questionnaires to participants.
- Have participant complete the BDI and the QOL questionnaires after the participant has eaten a light snack. The BDI should be scored as described in MOP Section 9.10.4 and notify the study physician and intervention leader if a problem exists so a suicide assessment may be conducted.
- Score the MAEDS questionnaire.
- Perform the BAM testing
- Alert psychologist if IDED-IV is needed.

Psychologist

- Conduct IDED-IV if needed**.** Can also be moved to Month 12 Visit 2 if cannot be fit into this visit if needed.

Physical Activity Measurements Technician

- Verify that the participant has not exercised or completed the VO2 Max in the past 24 hours.
- Proceed with muscle strength and endurance testing as described in MOP section 9.7.2.
- Notify staff that the participant is ready to continue with the next part of their visit. Send the participant back to the study coordinator.

Dietitian

- Instruct participants on 6-day food records as described in MOP section 9.5.
- Provide food record to participant.
- Verify that participant is taking supplements and has discontinued the use of any supplements that were not provided by the study.
- Notify staff that the participant is ready to continue the visit.

Study Coordinator

- Provide the control participant with a scale, weight log and instructions for measuring and recording their home weights as described in MOP section 9.3.4. Review with the CR participant the home weight procedures.
- Remind participant to bring their weight log to the next visit.
- Review participant binder and confirm that all procedures for this visit have been completed.
- Provide 3 month supply of vitamin/mineral and calcium supplements and perform pill count.
- Confirm date and time of the next Month 12 visit and remind the participant to bring their weight log to the clinic.

Research Assistant

- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to Study Manager to double check.

Study Manager

- Check all CRFs generated for Month 12 Visit 1 and approve.

8.7.4 Month 12 Visit 2 Preparation

The following materials are needed to conduct the Month 12 visit 2:

- Clinic Scales (Digital)
- DLW Urine Collection Kits
- 7-day PAR
- Food Records
- Weight Logs
- VO_2 Max Equipment
- IDED-IV (if needed and not performed at earlier Month 12 Visit)
- Adverse Event and Concomitant Medication Forms
- Results of safety laboratory tests
- Participant's Adverse Event Diary

8.7.5 Month 12 Visit 2 Conduction

Study Coordinator

- Greet the participant, and explain procedures for today's visit.
- Review the home weights log with the participant as described in MOP section 9.3.4. Return the weight log to the participant for further completion.
- Review the participant's diary and medications with the participant for any reported events. Proactively inquire if they experienced any health changes since the last visit.
- Perform the Stanford 7-day PAR as described in MOP section 9.7.3.
- Assess all adverse events and concomitant medication changes or new conditions and record on appropriate forms. See MOP sections 22.0 for further instructions.
- Take the participant and participant's binder to the DLW technician.
- Indicate the participant's last meal and what this was for the purpose of VO_2 testing
- Direct the participant to the VO2 Max testing area.
- Provide participant a meal after fasting procedures are completed, especially if there is extended testing at this visit.

Clinic Staff or Research Assistant

- Have the participant empty their bladder and weigh them on the CALERIE clinic scale prior to DLW urine collections.

DLW Technician

- Perform DLW Day 7 procedures as described in MOP section 10.0.

Dietitian

- Collect the participant's 6-day food record.
- Review the record for completeness including recording supplements.
- Remind subject to follow a high carbohydrate diet 3 days prior to OGTT during the in-patient stay

Physical Activity Measurements Technician

- Verify that the participant has not exercised or completed the muscle strength and endurance testing in the past 24 hours.
- Proceed with VO_2 Max testing as described in MOP section 9.7.1.
- Notify staff that the participant is ready to continue with the next part of their visit. Send the participant back to the study coordinator.

Physician

- Review safety laboratory test results and confirm that there are no concerns with participant safety.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.

Psychologist

- Perform IDED-IV (if needed)

Study Coordinator

- Review participant binder and confirm that all procedures for this visit have been completed.
- Confirm date and time of the next 12 Month visit and remind a participant not to exercise within 24 hours of next appointment. Also remind to bring weight log and diary to the clinic at next visit.

Research Assistant

- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the Study Manager.

Study Manager

- Check all CRFs generated for Visit 3 and approve.

8.7.6 Month 12 Visit 3 Preparation

The following materials are needed to conduct the Month 12 Visit 3:

- DTH toxoid and antigens
- High Carbohydrate Meal
- Core Temperature Capsule and Equipment
- Adverse Event and Concomitant Medication Forms

8.7.7 Month 12 Visit 3 Conduction

Inpatient Nursing Staff

- Admit participant to the inpatient unit by 4:00 pm
- Administer DTH (See MOP Section 9.9.1)

- Provide participant with the standard, high carbohydrate dinner prepared by the metabolic kitchen.
- Administer the core temperature capsule by 6:00 pm and document the time of administration. Oversee the attachment of the core temperature monitor for recording the core temperature over the next 24 hours. The monitor will be worn for a total of 26 hours after the capsule is swallowed, as an additional measure to obtain an accurate 24 hours core temperature recording. Please refer to MOP section 9.4.2 for further instructions.
- Review food records for high carbohydrate diet for the past 3 days.
- Remind the participant that he/she is required to fast overnight. Only water is allowed after dinner. Liquids must be at room temperature after ingestion of core temperature capsule.

Body Temperature Technician

- Perform core body temperature measurement as described in MOP section 9.4.2.

8.7.8 Month 12 Visit 4 Preparation

The following materials are needed to conduct the Month 12 visit 4:

- Clinic Scales (Digital)
- DLW Urine Collection Kits
- 24 Hour Urine Collection Container
- 7-day PAR
- Core Temperature Equipment
- RMR Equipment
- DTH 24-Hour Read
- Blood and Urine Collection Kits
- Blood/Urine for Archive
- OGTT Materials and Collection Kit
- Meals
- CANTAB
- Cognitive bias testing
- Home Weight Logs
- Participant's Diary for Review
- Adverse Event and Concomitant Medication Forms

8.7.9 Month 12 Visit 4 Conduction

Inpatient Nursing Staff

- Wake the participant at 7:00am and explain procedures for today's visit.
- Obtain clinic weight on CALERIE scale as described in MOP Section 9.3.1.
- Ask the participant to collect two separate DLW urine samples as directed in MOP section 10.0. Call the DLW Technician for pick-up after the collection of the 2 urine samples.
- Start 24 hour urine collection for isoprostanes after the DLW samples are collected. Instruct the participant how their urine should be collected and stored for the next 24 hours.

- Provide meals throughout the day as directed by the kitchen staff. **No meals should be served until the completion of the RMR, OGTT, and laboratory tests! All liquids must be served at room temperature during core temperature recording!**
- DTH 24 Hour Reading
- Take the core temperature monitor off the participant in 26 hours after the first signal was recorded as directed by the Body Temperature measurement technician.
- Provide overnight supervision for the participant.

DLW Technician

- Perform DLW Day 14 procedures as described in MOP section 10.0.

RMR Technician

- Verify that the participant is fasting and has not performed any physical activity in the last 48 hours.
- Perform RMR measurement as described in MOP Section 9.4.1.
- Take the participant and participant's binder to the coordinator.

Body Temperature Measurement Technician

- Verify that the participant is still wearing their core temperature monitor and inform the nursing staff when it is time for removal.

Study Coordinator

- Review and collect the home weights log with the participant as described in MOP section 9.4.3.
- Review participant's diary and medications with the participant for any reported events. Proactively inquire if they experienced any health changes since the last visit.
- Check that the final DLW samples have been collected and the 24 hour urine collection is in progress.
- Perform the Stanford 7-day PAR as described in MOP section 9.7.3.
- Take the participant and participant's binder to the phlebotomist or inpatient nurse.

Phlebotomist/ Inpatient Nurse

- Have the Month 12 visit outcome labs kit from the University of Vermont laboratory ready.
- Collect the outcomes blood samples, blood/urine for archive and take these to the local laboratory for processing and labeling for the University of Vermont lab as described in MOP Section 11.0. This will include extra aliquots for long term storage. (Samples that cannot be processed immediately must be stored under recommended conditions until processed).
- <u>Sex hormones (female participants only)</u>:
    1. Verify that a participant is in a mid-luteal phase (days 19-21, day one being the start of menses). If not, ask the study coordinator to reschedule blood collection. It should be planned for this when the visit is scheduled.
    2. Collect the first blood sample together with other outcome tests.

3. Collect a second blood samples one hour later.

- Take samples to the lab for processing and store samples under recommended conditions until they are shipped to the University of Vermont laboratory as described in MOP Section 11.0.
- Perform OGTT as described in MOP section 9.8.
- Ship samples to the laboratory as described in MOP Section 11.6.
- Document the shipment.
- Notify staff that the participant is ready to continue the visit.

Measurement Staff

- Perform the CANTAB testing after meal.
- Prepare the participant for Cognitive Function testing and complete testing.

Study Coordinator

- Review participant binder and confirm that all procedures for this visit have been completed.

Research Assistant

- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the study manager to double check.

Study Manager

- Check all CRFs generated for the inpatient stay and approve.

8.7.10 Month 12 Visit 5 Preparation

The following materials are needed to conduct the Month 12 visit 5:

- Muscle and Fat Biopsy Equipment and Sample Collection Kits
- DTH 48-Hour Read
- Lab Supplies for Sex Hormones (Females Only)
- Snack

8.7.11 Month 12 Visit 5 Conduction

Inpatient Nursing Staff

- Wake the participant at 7:00 am and explain procedures for today's visit.
- Provide meals throughout the day as directed by the kitchen staff.
- DTH 48 Hour Reading
- Discharge the participant after all visit procedures are completed.
- Assist physician in performing the biopsy. See section 9.9.1 for further instructions.

Study Coordinator

- Take the participant and participant's binder to the phlebotomist (females only)

- After participant completes the phlebotomy, take the participant's binder to the biopsy room.

Phlebotomist

- This is for female participants only!
- Have the Month 12 visit kit from the University of Vermont lab ready.
- Collect blood samples for sex hormones; take these to the local laboratory for processing, and labeling for the University of Vermont lab as described in MOP Section 11.0. (Samples that cannot be processed immediately must be stored under recommended conditions until processed).
- Store samples under recommended conditions until they are shipped to the laboratory as described in MOP Section 11.0.

Physician

- Perform muscle and abdominal fat biopsies as described in MOP section 13.0.

Study Coordinator

- Review participant binder and confirm that all procedures for this visit have been completed.
- Inform the inpatient staff that a participant could be discharged.
- Instruct the participant when to return to the clinic to meet with the intervention staff.

Research Assistant

- Complete any required CRF's for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the Study Manager to double check.

Study Manager

- Check all CRFs generated for this in-patient visit and approve.

8.7.12 Phone Follow-up for Biopsy Check Preparation

The following materials are needed to conduct the follow-up of the biopsy site:

- Progress note for verification of follow-up

8.7.13 Phone Follow-up for Biopsy Check Conduction

Study Coordinator

- Call participant 48 hours after biopsies to determine how sites are healing.
- Note this follow-up on a progress note and file this in the participant's binder.

8.8 Summary of Evaluations Performed for the CR Group During the Month 18 Visit Period

Month 18 Follow-Up (± 14 days)

Month 18 Visit 1 (Day 0)

Vital signs
Resting BP
Clinic weight
BMI Calculation
Waist Circumference
ECG
Urine Pregnancy Test (local lab)
Safety Labs: Blood Chemistry, Hematology and Urinalysis
Blood for antibody titers and archive
DLW Dose
DLW Urines
DXA
BMD/BMC
6-day Food Record - directions
Assessment of AE's and medication changes
Home weight instructions

Month 18 Visit 2 (Day 7)

Clinic weight
DLW Day 7 Urines
Home Weights (collect)
BDI
MAEDS
IDED-IV (If needed)
7-day PAR
6-day Food Record - review
Assessment of AE's and medication changes

Month 18 Visit 3 (Day 13)

Assessment of AE's and medication changes
Overnight Stay

Month 18 Visit 4 (Day 14)

Clinic weight
RMR
DLW Urines
Home Weights (Collect)
7-day PAR
Assessment of AE's and medication changes
Discharge

The study coordinator should contact the participant at least 1 month in advance to schedule or confirm scheduling of the Month 18 evaluations. Schedule all 4 visits at the

same time in order to confirm the correct spacing for DLW periods. Remind participant to refrain from taking their vitamin/mineral supplement the same day, prior to DXA testing.

8.8.1 Preparation and Conduction of Month 18 Visits for the CR Group

In some cases, the order of these procedures and tests can vary, however every effort should be made to keep all tests within the specified test day. Since the order of the visit may vary, a checklist will be used to monitor completion of these procedures and special notation will be made for items that must be done in a certain order. All staff members involved with the procedures must check off the appropriate box on the visit checklist that the procedure was completed. The study coordinator must verify that the checklist for that visit is complete at the end of each visit.

8.8.2 Month 18 Visit 1 Preparation (CR Group)

The following materials are needed to conduct the Month 18 visit 1:

- Clinic Scale (Digital)
- ECG Equipment
- BP Equipment
- Gulick II Tape Measure
- BMI calculator (CR group only)
- Digital Oral Thermometer
- Weight and vital signs form
- Weight log and directions
- Urine Pregnancy Test (local lab)
- Blood and Urine Collection Kits
- Blood Kit from Vermont Lab
- DLW Dose and Form
- DLW Urine Collection Kits
- DXA Machine
- Food Record Instructions and Food Records
- Adverse Event and Concomitant Medication Forms
- Participant's Adverse Event Diary
- 6 Month Supply Vitamin/Mineral and Calcium Supplements

8.8.3 Month 18 Visit 1 Conduction (CR Group)

Study Coordinator

- Greet the participant; confirm they are fasting for at least 12 hours (water is allowed). If not fasted, reschedule the visit.
- Explain procedures for today's visit and for the entire Month 18 testing period.
- Review the participant's diary and medications with the participant for any reported events. Proactively inquire if they experience any health changes since their last visit.
- Confirm the participant has not taken their vitamin/mineral supplement the same day, prior to DXA testing.

- Confirm the participant is not pregnant before taking participant and their binder to the DXA technician.
- Perform BMI calculation from weight/height measurements.
- Once the participant has completed the fasting procedures for the visit (weight and blood work), then provide the participant with a breakfast bar or other breakfast as specified at the site.
- Provide safety laboratory results upon receipt from the lab to the physician to review.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except undergarments.
- Have the participant void and obtain urine for local urine pregnancy testing. Have local lab run the test stat to obtain results prior to DXA testing.
- Bring the participant to the CALERIE scale and have the participant weigh in following the directions described in MOP section 9.3.1.
- Record weights on source document as directed in MOP section 9.3.1.
- Prepare patient for resting ECG and complete the ECG as directed in MOP section 9.12.
- Complete the waist circumference measurements as directed in MOP section 9.3.5.
- Prepare the participant for and perform resting heart rate and blood pressure measurements as described in section 9.2.3 and 9.2.4 of the MOP.
- Complete the remaining vital sign measurements (respiratory rate and oral temperature) as directed in MOP section 9.2.5.
- Bring the participant and the participant's binder to the phlebotomist for required blood/urine samples for archive.
- Assess all adverse events and concomitant medication changes or new conditions and record on appropriate forms. See MOP sections 22.0 for further instructions.

ECG Technician (may be certified study coordinator or in-patient staff)

- Record the ECG as directed in MOP section 9.12

Phlebotomist

- Have the Month 18 visit outcome and safety lab kits from LabCorp/Esoterix and the University of Vermont ready.
- Collect blood/urine for safety laboratory and blood for antibody titers and archive as directed in MOP section 12.0.
- Notify staff that the participant is ready to continue with the next parts of the visit.
- Take the samples to the lab for processing.
- Local laboratory processes and labels the samples and ships these to the safety lab. The certified phlebotomist oversees all procedures related to the safety and archive samples and shipping these to the appropriate labs.
- Local laboratory keeps inventory of shipment to the safety and Vermont labs.
- Document that samples were picked up.

DLW Technician

- Perform DLW Day 0 procedures as described in MOP section 10.0.

DXA Technician

- Perform the required DXA, BMD and BMC measurements as described in MOP section 9.6.1.
- Notify staff that the participant is ready to continue with the visit.

Study Coordinator

- Review the participant's diary and medications with the participant for any reported events. Proactively inquire if they experienced any health changes since their last visit.
- Provide weight log and directions.
- Review participant binder and confirm that all procedures for this visit have been completed.
- Provide 6 month supply of vitamin/mineral and calcium supplements and perform pill count.
- Confirm date and time of the next Month 18 visit and remind the participant to bring their weight log and events diary to the clinic.

Dietitian

- Instruct participants on 6-day food records as described in MOP section 9.5.
- Provide food record to participant.
- Verify that participant is taking supplements and has discontinued the use of any supplements that were not provided by the study.
- Notify staff that the participant is ready to continue the visit.

Physician

- Review vital signs, adverse events, concomitant medications and ECG, and confirm that there are no concerns with participant safety. Confirm the safety laboratory has actually been drawn at this visit.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.
- Notify staff that the participant is ready to continue the visit.

Research Assistant

- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to Study Manager to double check.

Study Manager

- Check all CRFs generated for Month 18 Visit 1 and approve.

8.8.4 Month 18 Visit 2 Preparation (CR Group)

The following materials are needed to conduct the Month 18 visit 2:

- Clinic Scale (Digital)
- DLW Urine Collection Kits

- BDI
- MAEDS
- IDED-IV (If needed)
- 7-day PAR
- Food Records
- Weight Logs
- Adverse Event and Concomitant Medication Forms
- Participant's Adverse Event Diary
- Results of safety laboratory tests

8.8.5 Month 18 Visit 2 Conduction (CR Group)

Study Coordinator

- Greet the participant, and explain procedures for today's visit.
- Review the home weights log with the participant as described in MOP section 9.3.4. Make one copy to be kept in the participant's binder and return the weight log to the participant for further completion.
- Review the participant's diary and medications with the participant for any reported events. Proactively inquire if they experienced any health changes since the last visit. See MOP Sections 22.0 for further instructions.
- Provide participant meal after fasting procedures for visit are completed and prior to psychological testing.
- Have staff notify Measurement Technician for testing.
- Perform the Stanford 7-day PAR as described in MOP section 9.7.3.
- Take the participant and participant's binder to the DLW technician.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except undergarments.
- Have participant empty bladder before weighing.
- Bring the participant to the CALERIE scale and have the participant weigh in following the directions described in MOP section 9.3.1.
- Record weights on source document as directed in MOP section 9.3.1.
- Inform Measurement Technician to perform testing

Measurement Technician

- Have participant complete the BDI and MAEDS. Score the BDI and the MAEDS questionnaire as described in MOP section 9.10, and notify study physician and intervention leader if a problem exists.

Psychologist

- Conduct IDED-IV if needed

DLW Technician

- Perform DLW Day 7 procedures as described in MOP section 10.0.

Dietitian

- Collect the participant's 6-day food record.
- Review the record for completeness including recording supplements.

Physician
- Review safety laboratory test results and confirm that there are no concerns with participant safety.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.

Study Coordinator
- Review participant binder and confirm that all procedures for this visit have been completed.
- Confirm date and time of the next Month 18 visit and remind the participant not to exercise within 24 hours of next appointment. Also remind them to bring weight log and diary to the clinic at next visit.

Research Assistant
- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the Study Manager.

Study Manager
- Check all CRFs generated for Visit 2 and approve.

8.8.6 Month 18 Visit 3 Preparation (CR Group)

The following materials are needed to conduct the Month 18 Visit 3:
- Adverse Event and Concomitant Medication Forms
- Participant's Adverse Event Diary

8.8.7 Month 18 Visit 3 Conduction (CR Group)

Clinic Staff
- Admit participant to the inpatient unit by 4:00 pm
- Remind the participant that he/she is required to fast overnight. Only water is allowed after dinner.

8.8.8 Month 18 Visit 4 Preparation (CR Group)

The following materials are needed to conduct the Month 18 visit 4:
- Clinic Scale (Digital)
- DLW Urine Collection Kits
- 7-day PAR
- RMR Equipment
- Meals
- Home Weight Logs

- Participant's Diary for Review
- Adverse Event and Concomitant Medication Forms

8.8.9 Month 18 Visit 4 Conduction (CR Group)

Inpatient Nursing Staff

- Wake the participant at 7:00am and explain procedures for today's visit.
- Take participant to clinic CALERIE scale and weigh participant.
- Provide the participant a gown and instruct them to remove all clothing except undergarments. Have participant empty their bladder before weighing.
- Have the participant weigh in following the directions described in MOP section 9.3.1.
- Record weights on source document as described in MOP section 9.3.1.
- Collect two separate DLW urine samples as directed in MOP section 10.0. Call the DLW Technician for pick-up after the collection of the 2 urine samples.
- Provide meals throughout the day as directed by the kitchen staff. **No meals should be served until the completion of the RMR!**
- Provide overnight supervision for the participant.

DLW Technician

- Perform DLW Day 14 procedures as described in MOP section 10.0.

RMR Technician

- Verify that the participant is fasting and has not performed any physical activity in the last 48 hours.
- Perform RMR measurement as described in MOP Section 9.4.1.
- Take the participant and participant's binder to the coordinator.

Study Coordinator

- Review and collect the home weights log with the participant as described in MOP section 9.3.1.
- Review participant's diary and medications with the participant for any reported events. Proactively inquire if they experienced any health changes since the last visit.
- Check that the final DLW samples have been collected.
- Perform the Stanford 7-day PAR as described in MOP section 9.7.3.

Research Assistant

- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the study manager to double check.

Study Coordinator

- Review participant binder and confirm that all procedures for this visit have been completed.
- Confirm date and time of Month 24 Visit.

Study Manager

- Check all CRFs generated for the in-patient stay and approve.

8.9 Summary of Evaluations Performed for the Control Group During the Month 18 Visit Period

Month 18 Follow-Up (± 14 days)

Month 18 Visit 1

Vital signs
Resting BP
Clinic weight
Waist Circumference
ECG
Safety Labs: Blood Chemistry, Hematology and Urinalysis
Blood for Antibody Titers and Archive
Assessment of AE's and medication changes
BDI
MAEDS
IDED-IV (If needed)
Discharge

The control participants do not undergo all of the evaluations that the CR participants do at the Month 18 visit; therefore there only needs to be one visit scheduled for them. The participant should be reminded a week prior to the scheduled visit to confirm the appointment.

8.9.1 Preparation and Conduction of Month 18 Visit for the Control Group

All staff members involved with the procedures must check off the appropriate box on the visit checklist that the procedure was completed. The study coordinator must verify that the checklist for that visit is complete at the end of the visit.

8.9.2 Month 18 Visit 1 Preparation (Control Group)

The following materials are needed to conduct the Month 18 visit 1:

- Clinic Scale (Digital)
- ECG Equipment
- BP Equipment
- Gulick II Tape Measure
- Digital Oral Thermometer
- Weight and vital signs form
- Blood and Urine Collection Kits
- Blood Kit from Vermont Lab
- Adverse Event and Concomitant Medication Forms
- Participant's Adverse Event Diary
- BDI questionnaire
- MAEDS and IDED-IV (if needed)
- 6 Month Supply of Vitamin/Mineral and Calcium Supplements

8.9.3 Month 18 Visit 1 Conduction (Control Group)

Study Coordinator

- Greet the participant and verify fasting status. Explain to the participant what will happen at today's visit.
- Review the participant's diary and medications with the participant for any reported events. Proactively inquire if they experience any health changes since their last visit.
- Once the participant has completed the fasting procedures for the visit (weight and blood work), then provide the subject with a meal as specified at the site.
- Provide safety lab results to the physician for review.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except undergarments.
- Bring the participant to the CALERIE scale and have the participant weigh in following the directions described in MOP section 9.3.1.
- Record weights on source document as directed in MOP section 9.3.1.
- Prepare patient for resting ECG and complete the ECG as directed in MOP section 9.12.
- Complete the waist circumference measurements as directed in MOP section 9.3.5.
- Prepare the participant for the resting heart rate and blood pressure measurements as described in section 9.2.3 and 9.2.4 of the MOP. Complete the heart rate and blood pressure measurements as described in the corresponding MOP sections.
- Complete the remaining vital sign measurements (respirations and temperature) as directed in MOP section 9.2.5.
- Notify Measurement Technician to complete BDI and MAEDS testing.
- Bring the participant and the participant's binder to the phlebotomy department for required blood work.

ECG Technician (may be certified study coordinator or in-patient staff)

- Record the ECG as directed in MOP section 9.12

Measurement Technician

- Have participant complete the BDI and MAEDS. Score the BDI and the MAEDS questionnaire as described in MOP section 9.10, and notify study physician and intervention leader if a problem exists.

Psychologist

- Conduct IDED-IV if needed

Phlebotomist

- Have the Month 18 visit outcome and safety lab kits from LabCorp/Esoterix and the University of Vermont ready.
- Collect blood/urine for safety and blood for antibody titers and archive as directed in MOP section 12.0.

- Notify staff that the participant is ready to continue with the next parts of the visit.
- Take the samples to the lab for processing.
- Local laboratory processes and labels the samples and will be shipping these to the safety and Vermont labs. The certified phlebotomist oversees all procedures related to the samples and shipping these to the safety lab.
- Local laboratory keeps inventory of shipment to the safety and Vermont labs.
- Document that samples were picked up.

Study Coordinator

- Review participant binder and confirm that all procedures for this visit have been completed.
- Provide the participant with 6 month supply of vitamin/mineral and calcium supplements and perform pill count.
- Confirm date/time of Month 24 visit.

Physician

- Review the vital signs and ECG. Confirm the safety laboratory tests have actually been drawn at this visit.
- Review the safety laboratory test results, when available, and confirm that there are no concerns with participant safety.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.

Research Assistant

- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to Study Manager to double check.

Study Manager

- Check all CRFs generated for Month 18 Visit 1 and approve.

8.10 Summary of Evaluations Performed for Both Groups During the Month 24 Visit Period

Month 24 Follow-Up (± 14 Days)

Month 24 Visit 1 (Day 0)

Urine Pregnancy Test (local lab)
Vital signs
Resting BP
Clinic weight
Waist Circumference
BMI Calculation (CR group only)
ECG
Safety Labs: Blood Chemistry, hematology, urinalysis
DLW Dose
DLW Urines
Physical Exam
DXA
BMD/BMC
QOL/Psychological Questionnaires:

- Rand SF-36, BDI, Profile of Moods States, PSS, PSQI, Derogatis, Food Cravings, FCI-II, Eating Inventory, WEL, MAEDS, BSQ

Body Acceptability Morph (BAM)
IDED-IV (if needed based on BAM and MAEDS may move to Month 24 Visit 2 if cannot be done at this visit)
Cybex (Muscle Strength)
6-day Food Record - directions
Assessment of AE's and medication changes
Issue home scale with directions (controls)

Month 24 Visit 2 (Day 7)

Clinic weight
DLW Day 7 Urines
Home Weights
7-day PAR
IDED-IV (if needed and no performed at earlier in Visit 1)
6-day Food Record - review
Assessment of AE's and medication changes
$V0_2$ Max

Month 24 Visit 3 (Day 13)

Vaccine Response prior to DTH administration
DTH
Standard Dinner (High Carbohydrate Meal) followed by overnight fast
Core Body Temperature – administer a capsule
Assessment of AE's and medication changes
Overnight Stay

Month 24 Visit 4 (Day 14)

RMR
Clinic weight
DLW Urines
Home Weights (Collect)
7-day PAR
Cognitive Function Measures
CANTAB
Core Body Temperature – complete the measurement
OGTT
Outcome laboratory tests, antibody titers and blood/urine for archive
Repeat Sex hormone – Females (1 hour after first sample)
DTH (24-hour read)
Overnight Stay
Assessment of AE's and medication changes

Month 24 Visit 5

Sex hormones – Females only
Muscle Biopsy (follow-up within 3 days to check that the site is healing)
Fat Biopsy
Adherence to Intervention
Assessment of AE's and medication changes
DTH (48-hour read)
Finish Questionnaires/Assessments
Discharge

Phone Follow-Up for Biopsy Check

Progress Note for phone follow-up

The study coordinator should contact the participant at least 1 month in advance to schedule or confirm scheduling of the Month 24 evaluations. Schedule all 5 visits at the same time in order to confirm the correct spacing for DLW periods. Remind participant to refrain from taking vitamin/mineral supplements the same day, prior to DXA testing.

8.10.1 Preparation and Conduction of Month 24 Visits

In some cases, the order of these procedures and tests can vary, however every effort should be made to keep all tests within the specified test day. Since the order of the visit may vary, a checklist will be used to monitor completion of these procedures and special notation will be made for items that must be done in a certain order. All staff members involved with the procedures must check off the appropriate box on the visit checklist that the procedure was completed. The study coordinator must verify that the checklist for that visit is complete at the end of each visit.

8.10.2 Month 24 Visit 1 Preparation

The following materials are needed to conduct the Month 24 visit 1:

- Clinic Scale (Digital)
- ECG Equipment

- BP Equipment
- Gulick II Tape Measure
- BMI Calculator (CR group only)
- Digital Oral Thermometer
- Weight and vital signs form
- Home Scales, Directions and Weight Logs
- Physical Exam Form
- Urine Pregnancy Test (local lab)
- Blood and Urine Collection Kits
- DLW Dose and Form
- DLW Urine Collection Kits
- DXA Machine
- QOL/Psychological Questionnaires
- BAM
- IDED-IV (if needed – may also be moved to Month 24 Visit 2 if needed)
- Muscle Strength and Endurance Equipment and Form
- Food Record Instructions and Food Records
- Adverse Event and Concomitant Medication Forms
- Participant's Event Diary

8.10.3 Month 24 Visit 1 Conduction

Study Coordinator

- Greet the participant; confirm they are fasting for at least 12 hours (water is allowed). If not fasted, reschedule the visit.
- Explain procedures for today's visit and for the entire Month 24 testing period.
- Review the participant's diary and medications with the participant for any reported events. Proactively inquire if they experience any health changes since their last visit.
- Confirm the participant has refrained from testing their vitamin/mineral supplements the same day, prior to DXA testing.
- Confirm that urine pregnancy test is negative for the upcoming DXA measurement.
- Notify clinic staff that the participant is ready for their procedures.
- Once the participant has completed the fasting procedures for the visit (weight and blood work), then provide the subject with a meal as specified at the site.
- Perform BMI calculation based on height/weight measurements.
- Provide safety laboratory results upon receipt from the lab to the physician to review.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except undergarments.
- Collect a urine sample for pregnancy testing and have participant empty bladder before weighing.
- Bring the participant to the CALERIE scale and have the participant weigh in following the directions described in MOP section 9.3.1.
- Perform pregnancy test stat so results can be obtained prior to DXA testing.

- Record weights on source document as directed in MOP section 9.3.1.
- Prepare patient for resting ECG and complete the ECG as directed in MOP section 9.12.
- Complete the waist circumference measurements as directed in MOP section 9.3.5.
- Prepare the participant for and perform resting heart rate and blood pressure measurements as described in section 9.2.3 and 9.2.4 of the MOP.
- Complete the remaining vital sign measurements (respiratory rate and oral temperature) as directed in MOP section 9.2.5.
- Bring the participant and the participant's binder to the phlebotomist for required blood work.
- Prepare participant for the physical exam.
- Confirm a negative urine pregnancy test for all applicable participants and send participant to have DXA.
- Send the participant to the muscle strength and endurance testing area.

ECG Technician (may be certified study coordinator or in-patient staff)

- Record the ECG as directed in MOP section 9.12

Phlebotomist

- Have the Month 24 visit safety labs kit from LabCorp/Esoterix ready.
- Collect blood and urine safety samples, process and label for safety lab as directed in MOP section 12.0.
- Notify staff that the participant is ready to continue with the next parts of the visit.
- Take the samples to the lab for processing.
- Local laboratory processes and labels the samples and ships these to the study safety laboratory. The certified phlebotomist oversees all procedures related to the safety samples and shipping these to the safety lab.
- Local laboratory keeps inventory of shipment to the safety lab.
- Document that samples were picked up.

DLW Technician

- Perform DLW Day 0 procedures as described in MOP section 10.0.

DXA Technician

- Perform the required DXA, BMD and BMC measurements as described in MOP section 9.6.1.
- Notify staff that the participant is ready to continue with the visit.

Dietitian

- Instruct participants on 6-day food records as described in MOP section 9.5.
- Provide food record to participant.
- Verify that participant is taking supplements and has discontinued the use of any supplements that were not provided by the study.
- Notify staff that the participant is ready to continue the visit.

Physician

- Review vital signs, adverse events, concomitant medications and ECG, and confirm that there are no concerns with participant safety. Confirm the safety laboratory has actually been drawn at this visit.
- Perform a physical examination to confirm continuing eligibility of the participant.
- Document physical exam results on the physical exam form provided by the study coordinator.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.
- Notify staff that the participant is ready to continue the visit.

Measurement Technician

- Have participant complete the BDI and the QOL questionnaires after the participant has eaten a light snack. The BDI should be scored as described in MOP Section 9.10.4 and notify the study physician and intervention leader if a problem exists so a suicide assessment may be conducted.
- Score the MAEDS questionnaire.
- Perform the BAM testing.
- Alert psychologist if IDED-IV is needed.

Psychologist

- Conduct IDED-IV if needed – may move to Month 24 Visit 2 if needed.

Physical Activity Measurements Technician

- Verify the participant has not exercised in the past 24 hours.
- Proceed with muscle strength and endurance testing as described in MOP section 9.7.2.
- Notify staff that the participant is ready to continue with the next part of their visit. Send the participant back to the study coordinator.

Study Coordinator

- For control participants, provide them with a scale. Provide a weight log and instructions for measuring and recording home weights as described in MOP section 9.3.4 for both groups.
- Remind all participants to bring their weight log to the next visit.
- Review participant binder and confirm that all procedures for this visit have been completed.
- Provide additional vitamin/mineral supplements as needed.
- Confirm date and time of the next Month 24 visit and remind the participant to bring their weight log and diary to the clinic.

Research Assistant

- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to Study Manager to double check.

Study Manager

- Check all CRFs generated for Month 24 Visit 1 and approve.

8.10.4 Month 24 Visit 2 Preparation

The following materials are needed to conduct the Month 24 visit 2:

- Clinic Scale (Digital)
- DLW Urine Collection Kits
- 7-day PAR
- Food Records
- Weight Logs
- VO2 Max Equipment
- IDED-IV (if needed and not performed at an earlier visit)
- Adverse Event and Concomitant Medication Forms
- Results of safety laboratory tests

8.10.5 Month 24 Visit 2 Conduction

Study Coordinator

- Greet the participant, and explain procedures for today's visit.
- Review the home weights log with the participant as described in MOP section 9.3.4.
- Review the participant's diary and medications with the participant for any reported events. See MOP Sections 22.0 for further instructions. Proactively inquire if they experienced any concerns with their health since the last visit.
- Perform the Stanford 7-day PAR as described in MOP section 9.7.3.
- Take the participant and participant's binder to the DLW technician.
- Indicate the participant's last meal and what this was for the purpose of VO_2 testing.
- Direct the participant to the VO_2 Max testing area.
- Provide participant a meal after fasting procedures are completed and especially before any extended psychological testing.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except undergarments.
- Bring the participant to the CALERIE scale and have the participant weigh in following the directions described in MOP section 9.3.1.
- Record weights on source document as directed in MOP section 9.3.1.

DLW Technician

- Perform DLW Day 7 procedures as described in MOP section 10.0.

Dietitian

- Collect the participant's 6-day food record.
- Review the record for completeness including recording supplements.
- Remind participant to follow a high carbohydrate diet for 3 days prior to OGTT during the in-patient stay.

Physical Activity Measurements Technician

- Verify that the participant has not exercised or completed the muscle strength and endurance testing in the past 24 hours.
- Proceed with VO2 Max testing as described in MOP section 9.7.1.
- Notify staff that the participant is ready to continue with the next part of their visit. Send the participant back to the study coordinator.

Physician

- Review safety laboratory test results and confirm that there are no concerns with participant safety.
- If there are safety concerns requiring further action, present a study coordinator with the action plan.

Psychologist

- Perform IDED-IV (if needed)

Study Coordinator

- Review participant binder and confirm that all procedures for this visit have been completed.
- Confirm date and time of the next Month 24 visit and remind the participant not to exercise within 24 hours of next appointment. Also remind to bring weight log and diary to the clinic at next visit.

Research Assistant

- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the Study Manager.

Study Manager

- Check all CRFs generated for Visit 2 and approve.

8.10.6 Month 24 Visit 3 Preparation

The following materials are needed to conduct the Month 24 Visit 3:

- Outcome Lab Kit to draw vaccine response
- DTH toxoid and antigens
- High Carbohydrate Meal
- Core Temperature Capsule and Equipment

8.10.7 Month 24 Visit 3 Conduction

Inpatient Nursing Staff

- Admit participant to the inpatient unit by 4:00 pm
- Insert heparin loc, have vaccine response titer drawn prior to DTH administration
- Provide participant with the standard, high carbohydrate dinner prepared by the metabolic kitchen.

- Administer the core temperature capsule by 6:00 pm and document the time of administration. Oversee the attachment of the core temperature monitor for recording the core temperature over the next 24 hours. The monitor will be worn for a total of 26 hours after the capsule is swallowed, as an additional measure to obtain an accurate 24 hours core temperature recording. Please refer to MOP section 9.4.2 for further instructions.
- Administer DTH (see MOP section 9.9.1).
- Remind the participant that he/she is required to fast overnight. Only water is allowed after dinner. All liquids should be at room temperature after ingestion of core temperature capsule.
- Review food records for high carbohydrate diet for the past 3 days.

Body Temperature Technician

- Perform core body temperature measurement as described in MOP section 9.4.2.

Phlebotomist

- Obtain vaccine response sample and refrigerate

8.10.8 Month 24 Visit 4 Preparation

The following materials are needed to conduct the Month 24 visit 4:

- Clinic Scale (Digital)
- DLW Urine Collection Kits
- 24 Hour Urine Collection Container
- 7-day PAR
- Core Temperature Equipment
- RMR Equipment
- Blood and Urine Outcome Collection Kits
- Blood/Urine Archive Kits
- OGTT Materials and Collection Kit
- Meals
- Cognitive Function Measures
- CANTAB
- Blood/Urine Archive Kits
- Home Weight Logs
- Participant's Diary for Review
- Adverse Event and Concomitant Medication Forms

8.10.9 Month 24 Visit 4 Conduction

Inpatient Nursing Staff

- Wake the participant at 7:00am and explain procedures for today's visit.
- Provide the participant with a gown and instruct them to remove all clothing except undergarments. Have participant empty bladder before weighing.
- Bring the participant to the CALERIE scale and have the participant weigh in following the directions described in MOP section 9.3.1.

- Record weights on source document as directed in MOP section 9.3.1.
- Ask the participant to collect two separate DLW urine samples as directed in MOP section 10.0. Call the DLW Technician for pick-up after the collection of the 2 urine samples.
- Start 24 hour urine collection for isoprostanes after the DLW samples are collected. Instruct the participant how their urine should be collected and stored for the next 24 hours.
- Provide meals throughout the day as directed by the kitchen staff. **No meals should be served until the completion of the RMR, OGTT, and laboratory tests! All liquids must be served at room temperature during core temperature recording!**
- Take the core temperature monitor off the participant in 26 hours after the first signal was recorded as directed by the RMR/Body Temperature measurement technician.
- Perform 24-hour DTH reading (see MOP section 9.9.1).
- Provide overnight supervision for the participant.

DLW Technician

- Perform DLW Day 14 procedures as described in MOP Section 10.0.

RMR Technician

- Verify that the participant is fasting and has not performed any physical activity in the last 48 hours.
- Perform RMR measurement as described in MOP Section 9.4.1.
- Take the participant and participant's binder to the coordinator.

Core Temperature Technician

- Verify that the participant is still wearing their core temperature monitor and inform the nursing staff when it is time for removal.

Study Coordinator

- Review and collect the home weights log with the participant as described in MOP section 9.3.4.
- Review participant's diary and medications with the participant for any reported events. Proactively inquire if they experienced any health changes since the last visit.
- Check that the final DLW samples have been collected and the 24 hour urine collection is in progress.
- Perform the Stanford 7-day PAR as described in MOP section 9.7.3.
- Take the participant and participant's binder to the phlebotomist or inpatient nurse.

Phlebotomist/ Inpatient Nurse

- Have the Month 24 visit outcome labs kit from the University of Vermont laboratory ready.
- Collect the outcomes blood samples, antibody titers and the blood and urine for archive and take these to the local laboratory for processing and labeling for the University of Vermont lab as described in MOP Section 11.0. This will include

extra aliquots for long term storage. (Samples that cannot be processed immediately must be stored under recommended conditions until processed).

- Sex hormones (female participants only):
  4. Verify that a participant is in a mid-luteal phase (days 19-21, day one being the start of menses). If not, ask the study coordinator to reschedule blood collection.
  5. Collect the first blood sample together with other outcome tests.
  6. Collect a second blood samples one hour later.
- Take samples to the lab for processing and store samples under recommended conditions until they are shipped to the University of Vermont laboratory as described in MOP Section 11.0.
- Perform OGTT as described in MOP section 9.8
- Ship samples to the laboratory as described in MOP Section 11.0.
- Document the shipment.
- Notify staff that the participant is ready to continue the visit.

Measurement Staff

- Perform the CANTAB testing after meal.
- Prepare the participant for Cognitive Function testing and complete testing.

Study Coordinator

- Review participant binder and confirm that all procedures for this visit have been completed.

Research Assistant

- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the study manager to double check.

Study Manager

- Check all CRFs generated for the in-patient stay and approve.

8.10.10 Month 24 Visit 5 Preparation

The following materials are needed to conduct the Month 24 visit 5:

- Muscle and Fat Biopsy Equipment and Sample Collection Kits
- DTH 48-Hour Read
- Lab Supplies for Sex Hormones (Females Only)
- Meal

8.10.11 Month 24 Visit 5 Conduction

Inpatient Nursing Staff

- Wake the participant at 7:00 am and explain procedures for today's visit.
- Provide meals throughout the day as directed by the kitchen staff.
- Perform 48-hour DTH reading (see MOP section 9.9.1).
- Discharge the participant after all visit procedures are completed.

- Assist physician in performing the biopsy. See section 9.9.1 for further instructions.

Study Coordinator
- Take the participant and participant's binder to the phlebotomist (if female), following then to the biopsy room.

Phlebotomist
- This is for female participants only!
- Have the Month 24 visit kit from the University of Vermont lab ready.
- Collect blood samples for sex hormones; take these to the local laboratory for processing, and labeling for the University of Vermont lab as described in MOP Section 11.0. (Samples that cannot be processed immediately must be stored under recommended conditions until processed).
- Store samples under recommended conditions until they are shipped to the Vermont laboratory as described in MOP Section 11.0.

Physician
- Perform muscle and abdominal fat biopsies as described in MOP section 13.0.

Study Coordinator
- Review participant binder and confirm that all procedures for this visit have been completed.
- Assess whether the participant had any adverse events during the inpatient stay.
- Collect all remaining vitamin/mineral supplements provided by the study and perform final pill count.
- Inform participant they may keep the home scale for continued home use.
- Inform the inpatient staff that a participant could be discharged.

Research Assistant
- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the Study Manager to double check.

Study Manager
- Check all CRFs generated for this inpatient visit and approve.

8.10.12 Phone Follow-up for Biopsy Check Preparation

The following materials are needed to conduct the 48-hour follow-up of the biopsy site:
- Progress note for verification of follow-up

8.10.13 Phone Follow-up for Biopsy Check Conduction

Study Coordinator
- Call participant to follow-up on biopsy sites and how these are healing
- Note this follow-up on a progress note and file this in the participant's binder.

8.11 Off-Schedule Evaluations

Certain study evaluations will be preformed at different time points or more frequently than the protocol specified Months 1, 3, 6, 9, 12, 18, and 24 visits.

8.11.1 Home Weights

Please refer to MOP Section 9.3.4 for details on home weights collection.

8.11.2 Responses to Vaccines

Standard doses of pneunococcal vaccine (PNU-Immune®23, Lederle Laboratories, Pearl River, NY), Hepatitis A (HAVRIX®, GlaxoSmithKline or VAQTA®, Merck and Co, Inc) and tetanus/diphtheria (DECAVAC, Aventis Pasteur) are to be administrated at Month 17 and a booster dose of hepatitis A vaccine to be administered at the Month 23 visit. Blood collection for antibody measurements is to be performed at baseline, Months 17, 18, 23 and 24.

8.11.2.1 Month 17

Study Coordinator

- Greet participant and verify they are fasting for at least 12 hours. If the participant is not fasting, reschedule the visit.
- Explain procedures for today's visit and answer any questions the participant may have.
- Document on a progress note that questions were addressed.
- If female, obtain urine specimen for pregnancy testing and run stat so results are confirmed prior to administering Hepatitis A vaccine.
- Make sure the participant emptied their bladder in preparation for the clinic weight measurement.
- Review the participant’s adverse event diary and current medications.

Clinic Staff or Research Assistant

- Provide the participant with a gown and instruct them to remove all clothing except for undergarments.
- Obtain stat pregnancy tests results, must be known before vaccination with Hepatitis A.
- Bring the participant to the clinic CALERIE scale and weigh the participant as described in MOP section 9.3.1.
- Record weights on source form as described in MOP section 9.3.1.
- Take the participant and participant’s binder to the phlebotomist

Phlebotomist/Clinic Nurse

- Have the Month 17 visit outcome labs kit from the University of Vermont laboratory ready.
- Collect blood samples as described in MOP section 11.0.

- Take blood samples to your local lab for processing and store samples under recommended conditions until they are shipped to the University of Vermont laboratory as described in MOP Section 11.0.
- Document the shipment.

Clinic Nurse
- Administer Hepatitis A booster vaccination as described in MOP Section 9.9.2.

Research Assistant
- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the Study Manager to double check.

Study Manager
- Check all CRFs generated for this inpatient visit and approve.

8.11.2.2 Month 23

Study Coordinator
- Greet participant and verify they are fasting for at least 12 hours. If the participant is not fasting, reschedule the visit.
- Explain procedures for today's visit.
- Address any questions and/or concerns the participant might have concerning the study or today's visit
- Document on a progress note that questions were addressed.
- Confirm local lab’s pregnancy test is negative prior to vaccination testing
- Review the participant adverse event diary and current medications.

Clinic Staff or Research Assistant
- Provide the participant with a gown and instruct them to remove all clothing except for undergarments.
- Obtain urine for local pregnancy testing and process stat.
- Bring the participant to the clinic CALERIE scale and weigh the participant as described in MOP section 9.3.1.
- Record weights on source form as described in MOP section 9.3.1.
- Take the participant and participant’s binder to the phlebotomist

Phlebotomist/Study Coordinator
- Have the Month 23 visit outcome labs kit from the University of Vermont laboratory ready.
- Collect blood as described in MOP section 11.0.
- Take blood samples to your local lab for processing and store samples under recommended conditions until they are shipped to the University of Vermont laboratory as described in MOP Section 11.0.
- Document the shipment.

Clinic Nurse

- Administer Hepatitis A booster vaccination as described in MOP Section XX.

Research Assistant

- Complete any required CRFs for this visit. Any CRF questions should be referred to the study coordinator.
- Give completed CRFs to the Study Manager to double check.

Study Manager

- Check all CRFs generated for this inpatient visit and approve.

8.11.2.3 Month 24

Please refer to MOP section 8.10.9 for details.

8.11.3 Laboratory Tests for Female Participants who Develop Amenorrhea During the Study

For female participants who develop amenorrhea for 2 months anytime during the study, FSH, LH and estrodiol will be drawn and sent to the University for Vermont laboratory. Any such event is an adverse event and must be appropriately documented.

Study Coordinator

- Following a report of amenorrhea, schedule a visit to the clinic as soon as possible.
- Greet participant and verify they are fasting for at least 12 hours. If the participant is not fasting, reschedule the visit.
- Explain procedures for today's visit.
- Address any questions and/or concerns the participant might have concerning the study or today's visit
- Document on a progress note that questions were addressed.
- Review the participant adverse event diary and current medications.
- Take the participant and participant's binder to the phlebotomist.

Phlebotomist/Study Coordinator

- Have the Unscheduled Visit labs kit from the University of Vermont laboratory ready.
- Collect blood samples as described in MOP section 11.0.
- Take blood samples to your local lab for processing and store samples under recommended conditions until they are shipped to the University of Vermont laboratory as described in MOP Section 11.0.
- Document the shipment.

Physician

- Review the laboratory test results and determine what further action is necessary.
- Present a study coordinator with the action plan.
- Provide an appropriate note for the participant's binder.

- Complete an Individual Discontinuation Report; if applicable please see MOP section 25.0).

Study Manager

- Assign responsibilities to appropriate staff members for implementing an action plan developed by physician-investigator.
- Ensure that all staff members are following an action plan developed by physician-investigator

8.11.4 Potassium Monitoring

For schedule, roles and responsibilities please refer to MOP section 24.1.

8.12 Evaluation Conducted on Drop-Outs and Withdrawals

Every effort should be made to keep participants in the study and schedule them for their return visits, even when the CR intervention has been temporarily or permanently discontinued. If withdrawal occurs for any reason, as many procedures as possible for the closest scheduled visit (Months 1, 3, 6, 9, 12, 18, or 24) must be performed. For details on the visits please refer to an appropriate subsection of section 8 of the MOP.

Month 1 Visit Checklist **CALERIE ID Number:_____**

Date of Visit: ___/___/___

Check completed items:

____Clinic Weight

____Resting BP

____Vital Signs

____BMI (CR Intervention Group only)

____Waist Circumference

____ECG

____Blood Chemistry, Hematology and Urinalysis

____BDI

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 3 Visit Checklist **CALERIE ID Number:_____**

Date of Visit: ___/___/___

Check completed items:

____Clinic Weight

____Home Weights

____Resting BP

____Vital Signs

____BMI (CR intervention group only)

____Waist Circumference

____ECG

____Blood Chemistry, Hematology and Urinalysis

____Blood for Archive

____BDI

____Review Concomitant Medications

____Review Adverse Events

____3 Month Supply of Vitamin/Mineral and Calcium Supplements Issued

Comments:

_____
_____
_____
_____
_____

Month 6 Visit Checklist **CALERIE ID Number:_____**
(CR Group)

Date of Visit 1: ___/___/___

Check completed items:

____Clinic Weight

____Resting BP

____Vital Signs

____BMI

____Waist Circumference

____ECG

____Blood Chemistry, Hematology and Urinalysis

____Review Concomitant Medications

____Review Adverse Events

____3 Month Supply of Vitamin/Mineral and Calcium Supplements Issued

Comments:

_____
_____
_____
_____
_____

Month 6 Visit Checklist **CALERIE ID Number:_____**
(CR Group)

Date of Visit 2: ___/___/___

Check completed items:

____Urine Pregnancy Test (local lab – STAT)

____Clinic Weight

____DLW Day 0 Procedures

____DXA (refrain from ingestion of vitamin/mineral supplements the same day, prior to DXA scan)

____BMD/BMC

____BDI

____MAEDS Questionnaire

____QOL Assessments

____Psychological Assessments

____BAM

____ IDED-IV (if Needed)

____6-day Food Record Instructions

____Provide Weight Log Instructions, and Weight Logs

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 6 Visit Checklist **CALERIE ID Number:_____**
(CR Group)

Date of Visit 3: ___/___/___

Check completed items:

____Clinic Weight

____DLW Day 7 Procedures

____Review 6-day Food Diary

____7-day PAR

____Review Home Weights Log

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 6 Visit Checklist **CALERIE ID Number:_____**
(CR Group)

Date of Visit 4: ___/___/___

Check completed items:

____Standard Meal Followed by Overnight Fast

____Administer Core Temp Capsule and Attach Monitor

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 6 Visit Checklist **CALERIE ID Number:_____**
(CR Group)

Date of Visit 5: ___/___/___

Check completed items:

____RMR

____Urine Pregnancy Test (local lab – STAT)

____Clinic Weight

____DLW Day 14 Procedures

____Blood for Bone Markers

____Blood for Archive

____Collect home weights log

____DXA (body comp) (refrain from ingestion of vitamin/mineral supplements the same day, prior to DXA scan)

____ Cognitive Function Measures

____ CANTAB

____Core Temperature (complete measurement)

____7-day PAR

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 6 Visit Checklist
(Control Group)

CALERIE ID Number:_____

Date of Visit 1: ___/___/___

Check completed items:

____Standard Dinner Followed by Overnight Fast

____Administer Core Temp Capsule and Attach Monitor

Comments:

_____
_____
_____
_____
_____

Month 6 Visit Checklist **CALERIE ID Number:_____**
(Control Group)

Date of Visit 2: ___/___/___

Check completed items:

____Clinic Weight

____Resting BP

____Vital Signs

____Waist Circumference

____ECG

____Blood Chemistry, Hematology and Urinalysis

____Blood for Archive

____Blood for Bone Markers

____BAM

____Cognitive Function Measurements

____MAEDS

____QOL Assessments

____Psychological Assessments

____ CANTAB

____ IDED-IV (if Needed)

____Core Temperature (complete measurement)

____Review Concomitant Medications

____Review Adverse Events

____3 Month Supply of Vitamin/Mineral and Calcium Supplements Issued

Comments:

_____
_____
_____
_____
_____

Month 9 Visit Checklist **CALERIE ID Number:_____**

Date of Visit: ___/___/___

Check completed items:

____Clinic Weight

____Resting BP

____Vital Signs

____BMI (CR intervention group only)

____Waist Circumference

____ECG

____Blood Chemistry, Hematology and Urinalysis

____BDI

____Review Concomitant Medications

____Review Adverse Events

____3 Month Supply of Vitamin/Mineral and Calcium Supplements Issued

Comments:

_____
_____
_____
_____
_____

Month 12 Visit Checklist **CALERIE ID Number:_____**

Date of Visit 1: ___/___/___

Check completed items:

____Urine Pregnancy Test (Local Lab – STAT)

____Clinic Weight

____Vital Signs

____Resting BP

____BMI Calculation (CR Group Only)

____Waist Circumference

____ECG

____Blood Chemistry, Hematology and Urinalysis

____DLW Day 0 Procedures

____Physical Exam

____DXA (refrain from ingestion of vitamin/mineral supplements the same day, prior to DXA scan)

____BMD/BMC

____Issue Home Scale/Weight Log with Directions (Control Group Only)

____QOL/Psychological Questionnaires

____ BAM

____ IDED-IV (if needed – may be moved to Month 12 Visit 2 if needed)

____Cybex (Muscle Strength)

____Issue Food Records with Directions

____Review Concomitant Medications

____Review Adverse Events

____6 Month Supply of Vitamin/Mineral and Calcium Supplements Issued

Comments:

Month 12 Visit Checklist **CALERIE ID Number:_____**

Date of Visit 2: ___/___/___

Check completed items:

____Clinic Weight

____DLW Day 7 Procedures

____Collect Home Weights

____7-Day PAR

____Collect 6 day Food Record

____VO2 Max (indicate participant's last meal and what this was prior to testing _____)

____IDED-IV (if needed)

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 12 Visit Checklist **CALERIE ID Number:_____**

Date of Visit 3: ___/___/___

Check completed items:

____Administer DTH

____Standard Dinner (High Carbohydrate Meal) Followed by Overnight Fast

____Administer Core Temperature Capsule and Attach Monitor

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 12 Visit Checklist **CALERIE ID Number:_____**

Date of Visit 4: ___/___/___

Check completed items:

____RMR

____Clinic Weight

____DLW Day 14 Procedures

____Collect Home Weights

____7-day PAR

____Core Temperature (complete measurement)

____OGTT

____Lab Work: Cardiovascular Risk Factors, insulin, C-peptide, sex hormones, endocrine response and growth factors, bone markers, blood/urine for archive

____MAEDS Questionnaire

____Cognitive Function Measurements

____ CANTAB

____Repeat Sex hormone – Females (1 hour after first sample)

____DTH (24-hour read)

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 12 Visit Checklist **CALERIE ID Number:_____**

Date of Visit 5: ___/___/___

Check completed items:

____Sex hormones – Females only

____Muscle Biopsy

____Fat Biopsy

____DTH (48-hour read)

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 12 Phone Visit Checklist (48 – 72 hours after biopsies)

Date of Phone Call: ___/___/____

____Phone Follow-Up for Biopsy Check

____Progress Note for Phone Follow-up

Comments:

_____
_____
_____
_____
_____

Month 18 Visit Checklist **CALERIE ID Number:_____**
(CR Group)

Date of Visit 1: ___/___/___

Check completed items:

____Urine Pregnancy Test (local lab STAT)

____Clinic Weight

____Resting BP

____Vital Signs

____BMI Calculation (CR group only)

____Waist Circumference

____ECG

____Blood Chemistry, Hematology and Urinalysis

____Blood for Antibody Titers and Archive

____DLW Dose 0 Procedures

____DXA (refrain from ingestion of vitamin/mineral supplements the same day, prior to DXA scan)

____BMD/BMC

____Directions for 6-day Food Record

____Home weight Instructions

____Review Concomitant Medications

____Review Adverse Events

____6 Month Supply of Vitamin/Mineral and Calcium Supplements Issued

Comments:

_____
_____
_____
_____
_____

Month 18 Visit Checklist **CALERIE ID Number:_____**
(CR Group)

Date of Visit 2: ___/___/___

Check completed items:

____Clinic Weight

____DLW Day 7 Urine Procedures

____Collect Home Weights

____BDI

____MAEDS

____ IDED-IV (if Needed)

____7-day PAR

____Collect 6 day Food Record

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 18 Visit Checklist (CR Group) **CALERIE ID Number:_____**

Date of Visit 3: ___/___/___

Check completed items:

____Standard Dinner Followed by Overnight Fast

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 18 Visit Checklist (CR Group) **CALERIE ID Number:_____**

Date of Visit 4: ___/___/___

Check completed items:

____RMR

____Clinic Weight

____DLW Day 14 Urine Procedures

____Collect Home Weights

____7-day PAR

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 18 Visit Checklist **CALERIE ID Number:_____**
(Control Group)

Date of Visit: ___/___/___

Check completed items:

____Clinic Weight

____Resting BP

____Vital Signs

____Waist Circumference

____ECG

____Blood Chemistry, Hematology and Urinalysis

____Blood for Archive

____BDI

____MAEDS

_____ IDED-IV (if Needed)

____Review Concomitant Medication

____Review Adverse Events

____6 Month Supply of Vitamin/Mineral and Calcium Supplements Issued

Comments:

_____
_____
_____
_____
_____

Month 24 Visit Checklist **CALERIE ID Number:_____**

Date of Visit 1: ___/___/___

Check completed items:

____Urine Pregnancy Test (local lab STAT)

____Clinic Weight

____Resting BP

____Vital Signs

____Waist Circumference

____BMI Calculation (CR group only)

____ECG

____Blood Chemistry, Hematology and Urinalysis

____DLW Day 0 Procedures

____Physical Exam

____DXA (refrain from ingestion of vitamin/mineral supplements the same day, prior to DXA scan)

____BMD/BMC

____QOL/Psychological Questionnaires

____ BAM

____IDED-IV (If needed – may be moved to Month 24 Visit 2 if needed)

____Cybex (Muscle Strength)

____Directions for 6-day Food Record

____Issue home scale with directions (controls)

____Review Concomitant Medications

____Review Adverse Events

____Vitamin/Mineral and Calcium Supplements Issued

Comments:

Month 24 Visit Checklist **CALERIE ID Number:_____**

Date of Visit 2: ___/___/___

Check completed items:

____Clinic Weight

____DLW Day 7 Urines

____Review Home Weights Log

____7-day PAR

____Collect 6 day Food Record

____V02 Max (indicate the participant's last meal and what this was prior to testing _____)

____IDED- IV (if needed)

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 24 Visit Checklist **CALERIE ID Number:_____**

Date of Visit 3: ___/___/___

Check completed items:

____Vaccine Response (obtain titer sample prior to DTH administration)

____Administer DTH

____Standard Dinner (High Carbohydrate Meal) Followed by Overnight Fast

____Administer Core Temperature Capsule and Attach Monitor

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 24 Visit Checklist **CALERIE ID Number:_____**

Date of Visit 4: ___/___/___

Check completed items:

____RMR

____Clinic Weight

____DLW Day 14 Urine Procedures

____Collect Home Weights

____7-day PAR

____Core Temperature (complete measurement)

____OGTT

____Lab Work: Cardiovascular Risk Factors, insulin, C-peptide, sex hormones, endocrine response and growth factors, bone markers, blood/urine for archive

____Repeat Sex hormone – Females (1 hour after first sample)

____DTH (24-Hour Read)

____Cognitive Function Measurements

____ CANTAB

____Review Concomitant Medications

____Review Adverse Events

Comments:

_____
_____
_____
_____
_____

Month 24 Visit Checklist **CALERIE ID Number:_____**

Date of Visit 5: ___/___/___

Check completed items:

____Sex hormones – Females only

____Muscle Biopsy

____Fat Biopsy

____Adherence to Intervention

____DTH (48-hour read)

____Review Concomitant Medications

____Review Adverse Events

____Collect Vitamin/Mineral and Calcium Supplements

Comments:

_____
_____
_____
_____
_____

Month 24 Phone Visit Checklist (48 – 72 hours after biopsies)

Date of Phone Call: ___/___/____

____Phone Follow-Up for Biopsy Check

____Progress Note for phone follow-up

Comments:

_____
_____
_____
_____
_____