3. SOURCES OF DATA

Data for the central database will come from a variety of sources and include the following.

- Basic clinical information and data obtained from outcome assessments performed at each site, i.e., screening and eligibility criteria, demographic information, vital signs and physical measures, metabolic measures, food intake, food pattern and physical activity assessments, the results of the physical examinations, adverse events, quality of life and cognitive function questionnaires, etc., will be recorded on paper case report forms (CRFs).
- Laboratory tests, i.e., serum lipids and lipoproteins, inflammatory markers, insulin and glucose, immune function, endocrine response, etc., will be performed by a central biochemistry laboratory. Additionally, serum lipids and lipoproteins, CRP, fasting blood glucose and insulin will be performed by the safety laboratory at BL, Month 12 and Month 24 for the purpose of sharing results with participants. Electronic files will be transferred to the CC using a secure FTP server and merged into the main CALERIE database.
- Safety laboratory tests, i.e., potassium, hemoglobin, hematocrit, etc., will be performed by a second central biochemistry laboratory. Electronic files will be transferred to the CC using a secure FTP server and merged into the main CALERIE database.
- Urine samples from study participants will be forwarded to the central DLW reading center at Baylor University. Electronic files with the resulting DLW measures will be forwarded to the CC using a secure FTP server and merged into the main CALERIE database.
- DXA files will be forwarded to the central DXA reading center for reading and interpretation. Electronic files with the resulting body composition measures will be forwarded to the CC using a secure FTP server and merged into the main CALERIE database.
- Six-day food record data will be recorded on paper data forms and forwarded to a dietary coding center. There, they will be entered into a database using the Nutritional Data System (NDS). Electronic files with the nutrition analysis will be forwarded to the CC using a secure FTP server and merged into the main CALERIE database.

In all cases, data for a particular participant will be identified by the CALERIE ID number, the protocol time point and the date of the corresponding procedure so that they can be merged successfully in the CALERIE database.

3.1 Data Management Activities

All data management activities and data quality at the DCRI will be guided by a comprehensive set of data management Standard Operating Procedures (SOPs). At the time of writing, there are 22 written procedures covering all areas starting with CRF receipt and entry, through database lock. The SOPs provide a detailed description of every staff member's roles and responsibilities in each step of the data management process, regulate data base development, describe internal audit procedures, data audit trail, data status reports, version control measures, and training requirements. In general, the following data management procedures will be applied.

1. Paper Case Report Forms (CRFs) will be designed specifically for this study. They will be designed to capture all the information required to address the reports and analyses described above.
1. Appropriate conventions for specific data fields will be defined according to the according to the DCRI's standard operating procedures (SOPs). They include, for example, conventions for text fields, numeric fields, Yes/No fields, date fields, checklists, and missing data.
2. Key fields, e.g., the participant's ID number, the protocol time point and date of the evaluation, will be recorded for each major component of the CRF.
3. Personnel at clinical sites will record the data mandated by the study on the CRFs. Every CRF page will be accompanied by detailed instructions to promote consistency and reliability across the sites and over time. All CRFs will be completed according to the current Good Clinical Practices (GCP) guidelines [283,284]. Training on completing (and correcting) the CRFs as well as forwarding them to the CC will be included in the initial training session and any follow-up training sessions.
4. At periodic intervals, a copy of the CRF will forwarded to the CC by parcel delivery service for data entry and processing.
5. As described above, a variety of supplementary material and procedures will be conducted with study participants, including blood and urine samples, DXA evaluations and the dietary recall. The resulting files and/or materials will be forwarded directly to central laboratories and reading centers for processing and interpretation.
6. A database will be created on the DCRI computer network specifically for this study. As described above, the database will be managed with Oracle using Clintrial for data entry.
7. Each record in the database is identified by the participant's ID, the protocol time point and a unique record identifier.
8. CRFs forwarded from the clinical sites will be entered into the study database. Double data entry, by two different operators at two separate occasions, will be performed [285-287] to ensure a high level of confidence in the data entered.
9. Similarly, a data dictionary will include information for each of the electronic data records. Each record type will be designed to integrate with the rest of the database. Key fields will specifically be identified for these records.
10. At periodic intervals, these electronic data files will be forwarded to the CC using a secure FTP server. From there, they will be merged into the master database according to the DCRI's SOPs.

11. A series of validation checks will be developed for the database. They will search for impossible and implausible values as well as logical inconsistencies across the different data fields; longitudinal checks will evaluate consistency in variables over time; other checks will search for digit preferences or peculiar or fabricated values. For any exception uncovered, a data clarification form (DCF) will be generated and forwarded to the clinical site for investigation and resolution. Corrections will be made on the DCF and returned to the CC for data entry.
12. If a correction is required to the original CRF prior to submission to the CC, it will be made according to GCP guidelines. That is, a single line will be drawn through the old value so that the original entry is still visible. The correct value will be written close to the field, and the correction initiated and dated by the CALERIE staff member at the site making the change.

3.2 Schedule of Evaluations

CALERIE Evaluation	Screen-ing	Baseline	Follow-up Month						
			1	3	6	9	12	18	24
Screening Procedures (Section Error! Reference source not found.**):**									
Telephone Screen: Age; Height, Weight ⇒ BMI Inclusion Criteria	**X**								
Screening Informed Consent and HIPAA Authorization	**X**								
Demographic Information	**X**								
Exclusion Criteria (Section **Error! Reference source not found.**):									
*Medical and Medication History (Section **Error! Reference source not found.**)*	X								
Abbreviated Medical and Medications History		X							
Screening Questionnaires (Eating Inventory, MAEDS, SCID II, Personality Q're, BDI, GHQ, Body Morph test, IDED-IV)	X								
*Serum Pregnancy Test for Women (Section **Error! Reference source not found.**)*	X								
Barriers to Participation, Diet Preferences, Allergies, Special Conditions	X								
14-day Food Record	X								
Study Informed Consent and HIPAA Authorization		**X**							
Vital Signs (Section Error! Reference source not found.**)**		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Clinic Height (Section Error! Reference source not found.**)**		**X**							
Clinic Weight (Section Error! Reference source not found.**,** Error! Reference source not found.**)**		**X**	**X**	**X**	**X****	**X**	**X****	**X****	Mo.17, 18,23,24

CALERIE Evaluation	Screen-ing	Baseline	Follow-up Month						
			1	3	6	9	12	18	24
Home Diaries, i.e., Weight, Food, Symptoms (Section Error! Reference source not found. **&** Error! Reference source not found.**)**		**X**	**Daily**						
Energy Metabolism (Section Error! Reference source not found.**):**									
TEE by DLW		XX			X*		X	X*	X
RMR		XX			X*		X	X*	X
Core Body Temperature		X			X		X		X
Cardiovascular Risk Factors (Section Error! Reference source not found.**):**									
Resting Blood Pressure		X	X	X	X	X	X	X	X
Lipids, Markers of Inflammation, CRP, TGF, etc.		X					X		X
Glucose Tolerance and Insulin (Section Error! Reference source not found.**):**									
OGTT, insulin and C-peptide		X					X		X
Immune Function:									
DTH (Section **Error! Reference source not found.**)		X					X		X
Antibody Response to Vaccines (Section **Error! Reference source not found.**)		X							Mo.17, 18,23,24
Endocrine Response and Growth Factors (Section Error! Reference source not found.**):**									
Norepinephrine, DHEA, Sex Hormones (for men), Thyroid Hormones, Adipokines, Angiotensin II, Growth Hormone & Growth Factors		X					X		X
QoL, Psychological, Cognitive Function (Section Error! Reference source not found.**)**		**X**			**X**		**X**		**X**
Physical Activity Measurements (Section Error! Reference source not found.**):**									

CALERIE Evaluation	Screen-ing	Baseline	Follow-up Month						
			1	3	6	9	12	18	24
Stanford 7-day PAR	X	XX			X*		X	X*	X
Maximal Oxygen Uptake (VO_{2max})		X					X		X
Muscular Strength and Endurance		X					X		X
Body Composition (Section Error! Reference source not found.**):**									
Waist Circumference		X	X	X	X	X	X	X	X
DXA, including BMD and BMC		XX			XX*		X	X*	X
Markers of Bone Turnover (Section Error! Reference source not found.**)**		**X**			**X**		**X**		**X**
Nutrient Intake (Section Error! Reference source not found.**)**	**X**	**XX**			**X***		**X**	**X***	**X**
Archive Materials (Section Error! Reference source not found.**):**									
Blood		X		X	X		X	X	X
Urine		X					X		X
Muscle and Abdominal Fat Biopsy		X					X		X
Concomitant Medications (Sections Error! Reference source not found.**,** Error! Reference source not found.**,** Error! Reference source not found.**)**		**X**	**X**	**X**	**X**	**X**	**X**	**X**	Mo.17, 23,24
Participant Safety:									
Blood Chemistry, Hematology and Urinalysis (Section **Error! Reference source not found.**)	X	X	X	X	X	X	X	X	X
Urine Pregnancy Test for Women (Sections **Error! Reference source not found.** and **Error! Reference source not found.**)		X			X*		X	X*	Mo.17, 23, 24
Adverse Events (Section **Error! Reference source not found.**, **Error! Reference source not found.**)		X	X	X	X	X	X	X	Mo.17, 23,24

CALERIE Evaluation	Screen-ing	Baseline	Follow-up Month						
			1	3	6	9	12	18	24
Serious Adverse Events (Section **Error! Reference source not found.**)			As they occur with an expedited reporting protocol						
Physical Examination (Section **Error! Reference source not found.**)	X	X					X		X
Potassium Surveillance, ECG, Creatine Phosphokinase (Section **Error! Reference source not found.**)	X	X	X	X	X	X	X	X	X
Anemia Screening / Surveillance (Section **Error! Reference source not found.**)	X	X	X	X	X	X	X	X	X
Cholesterol Surveillance (Sections **Error! Reference source not found.** and **Error! Reference source not found.**)	X	X					X		X
Eating Disorders Screening / Surveillance (Section **Error! Reference source not found.**)	X	X		X	X		X	X	X
BMI Screening / Surveillance (Section **Error! Reference source not found.**)	X		X	X*	X*	X*	X*	X*	X*
BDI Screening / Surveillance (Section **Error! Reference source not found.**)	X	X	X	X	X	X	X	X	X
DXA scans of hip and spine		X			X*		X		X