Framingham State Food Study (FS)^2
FUNDING OPPORTUNITY ANNOUNCEMENT (FOA)

This FOA solicits applications for funding to conduct ancillary studies in conjunction with the Framingham State Food Study (FS)^2. This major research initiative will involve random assignment of 150 students, faculty, and staff to 1 of 3 weight-loss maintenance diets, varying in carbohydrate and fat. Implementation of the study is planned for the 2014/5 and 2015/6 academic years, followed by a period of data analysis and interpretation. See attached *Overview of Parent Project* for details.

Approximately $30,000 is available for distribution among 3 to 5 ancillary studies, with total costs not exceeding $10,000 per study. The goal of this FOA is to provide research opportunities that advance scientific knowledge by taking advantage of the infrastructure of the parent project. The ancillary study can address any area broadly related to nutrition and health. Secondary goals of this FOA are to promote collaboration between the FSU academic community and researchers from Boston Children's Hospital (BCH), and to provide on-campus research opportunities for faculty and educational experiences in research for students.

Examples of possible topics for ancillary studies are listed below. This is not an exhaustive list. Innovative ideas are encouraged.

- Impact of the parent study on nutrition awareness and lifestyle behaviors throughout the FSU community
- Development of a smart phone application to assess food intake in a university setting
- Methods to enhance social support for adhering to the rigors of participation in a controlled feeding study
- Systematic evaluation of reasons for continuing or discontinuing study participation

Eligibility and Restrictions Any current FSU faculty member may apply. Funding can be used for any related research expense (e.g., student or post-doctoral stipend, research assistant salary, laboratory costs), except salary for the Principal Investigator. No more than one letter of intent may be submitted by any Principal Investigator.

Evaluation Criteria A committee comprising members of the research team at BCH and faculty and administrators from FSU will evaluate letters of intent and full applications. Criteria will include scientific merit, public health significance, innovation, approach, relevance to the parent project, and feasibility. Additional considerations will include incremental burden on study participants, risk to study participants, adequacy of proposed budget, and likelihood for successful completion.

Publication Considerations It is expected that the Principal Investigator of the ancillary study will be the first or last author of the manuscript describing the results of the ancillary study. Please carefully consider the timeline for the parent project when considering how completion of the proposed ancillary study may contribute to credit for promotion and tenure. The research team at BCH will discuss terms of publication with the Principal Investigator of each funded ancillary study. Timing of publication will depend, in part, on the aim(s) of the ancillary study.

Regulatory Considerations The Principal Investigator of each ancillary study will work with the research team at BCH to obtain approval from the Committee on Clinical Investigation at BCH (i.e., Institutional Review Board IRB), which is overseeing ethical conduct of the parent project.

Timeline

March 24, 2014: Letter of Intent (1-page limit) due at 5:00 pm.

April 11, 2014: Full applications invited for selected ancillary studies

May 16, 2014: Full applications (5-page limit, not including references) due at 5:00 pm

May 30, 2014: Funding decision announced. Recipients will be expected to work with the BCH-FSU research team over the summer of 2014 to ensure that the ancillary study is appropriately integrated into the parent project.

APPLICATION INSTRUCTIONS

Use provided electronic templates for the Letter of Intent and Full Application.

Do not exceed specified page limits, with the font remaining at Arial 11 and 0.5-inch margins.

Letter of Intent *(1 page)*

Background Include a brief evaluation of previous research and include any additional background information providing rationale for the proposed ancillary study. Specifically identify the research gap that the project is intended to address.

Aims and Hypotheses Succinctly state the aims and corresponding hypotheses.

Outcomes List the outcomes for the proposed ancillary study and briefly describe assessment methods in the context of the parent project.

Significance Highlight the public health or clinical significance of the proposed ancillary study to public health.

Anticipated Budget Provide the total direct costs for the proposed ancillary study.

Disclosures Summarize any potential conflict(s) of interest that might be related to the proposed area of research.

Full Application

Abstract Provide a brief summary of the primary hypothesis and research question (not exceeding 2,000 characters, including punctuation and spaces).

Budget Describe budget items, according to the categories specified in the form, and include an estimate of costs.

Biographical Sketch Submit a biographical sketch for the Principal Investigator. Note that the format is generally consistent with the format specified by the National Institutes of Health, with some adaptations for this FOA.

Disclosures Include full disclosure of any potential conflict(s) of interest that might be related to the proposed area of research. Questions are consistent with those required on the Form for Disclosure of Potential Conflicts of Interest, issued by the International Committee of Medical Journal Editors.

Research Plan (5 pages)

Study Aims and Hypotheses (1 page) *S*tate the Primary Aim and any Secondary Aims, with the hypothesis(es) and study outcomes for each Aim. Describe the public health or clinical significance of the proposed study.

Background (1 page) Summarize prior studies and rationale for proposed study.

Study Outcomes and Assessment Methods (2 pages) Describe study outcomes and methods for assessing these outcomes. Address how the assessment protocols might impact study logistics and feasibility. Consider safety.

Statistics (1/2 page) Include a sample size calculation as well as a preliminary analysis plan.

Limitations (1/2 page) Describe recognized limitations of the proposed study.

References (1 page) List citations.

Questions For any questions regarding this FOA, please contact Cara Ebbeling, PhD by telephone (617-919-3457) or Email (cara.ebbeling@childrens.harvard.edu).

Submit Letter of Intent to:

Daniele Skopek, Program Manager
New Balance Foundation Obesity Prevention Center, Boston Children's Hospital
daniele.skopek@chldrens.harvard.edu

OVERVIEW OF PARENT PROJECT

Dietary Composition and Energy Expenditure during Weight-Loss Maintenance

Principal Investigators – Cara B. Ebbeling, PhD – David S. Ludwig, MD, PhD – Boston Children's Hospital

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Many overweight and obese people can lose weight for a few months, but most have difficulty maintaining weight loss over the long term. One explanation for the poor long-term outcome of conventional diets is that weight loss causes biological adaptations that promote weight regain. We recently examined this question in a feeding study with 21 overweight or obese young adults, with each of three popular diets consumed for a four-week period. We found that study participants "burned" 325 more kcal on a low-carbohydrate diet compared to a conventional diet (*Ebbeling et al. JAMA 2012*). We also observed important dietary effects on insulin resistance, cortisol excretion, and other chronic disease risk factors. The purpose of the upcoming study at FSU is to follow-up our initial findings using a greater number of volunteers studied over a longer time period, to yield definitive results. Following 12 ± 2% weight loss on a standard run-in diet for approximately 12 weeks, 150 young adults (students, faculty, staff) will be randomly assigned to one of three weight-loss maintenance diets (low-, moderate-, or high-carbohydrate) for 20 weeks (Figure 1). The dining services at FSU will prepare and serve meals and snacks corresponding to each of the diets, representing a novel approach to conducting a controlled feeding study. Each participant will be enrolled in the study for one academic year.

Specific Aim #1: To evaluate the effects of 3 diets varying widely in carbohydrate-to-fat ratio (high-carbohydrate, moderate-carbohydrate, low-carbohydrate) on energy expenditure during weight-loss maintenance.

Hypotheses

1a Total energy expenditure during weight-loss maintenance will differ among test diets at 20 weeks.

1b Resting energy expenditure during weight-loss maintenance will differ among test diets at 20 weeks.

Primary outcome: total energy expenditure (assessed by indirect calorimetry using stable isotopes).

Secondary outcomes: dietary energy required to maintain weight stability following weight loss, resting energy expenditure (assessed by indirect calorimetry using respiratory gas exchange), and physical activity (assessed by accelerometry).

Specific Aim #2: To evaluate the effects of 3 diets varying widely in carbohydrate-to-fat ratio on chronic disease risk factors during weight-loss maintenance.

Hypothesis

2 Chronic disease risk factors during weight-loss maintenance will differ among test diets at 20 weeks.

Secondary outcomes: insulin sensitivity and insulin secretion (assessed by frequently-sampled oral glucose tolerance test, OGTT), glycemic control (HgA1c), lipid profiles (total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides), coagulopathy (PAI-1, fibrinogen), inflammatory mediators (CRP, IL-6), fasting leptin, endothelial dysfunction (number and function of endothelial progenitor cells), and blood pressure.

Specific Aim #3: To evaluate physiological mechanisms potentially relating dietary carbohydrate-to-fat ratio to metabolism and risk for chronic disease – including CVD, type 2 diabetes, and cancer.

Hypothesis

3 Differences among diets in measures of skeletal muscle work efficiency, insulin sensitivity and secretion, body composition, anabolic and catabolic hormones, and gut microbiome will provide additional physiological insights into the effects of dietary composition on health outcomes during weight-loss maintenance.

Secondary outcomes: skeletal muscle work efficiency (assessed by cycle ergometry), body composition, insulin sensitivity and secretion, thyroid functions (free T4, rT3, TSH), growth hormone action (IGF-1, IGF binding proteins), reproductive hormones (LH, FSH, testosterone, estradiol), stress hormones (24-hour urinary cortisol and catecholamines), and gut microbiome.

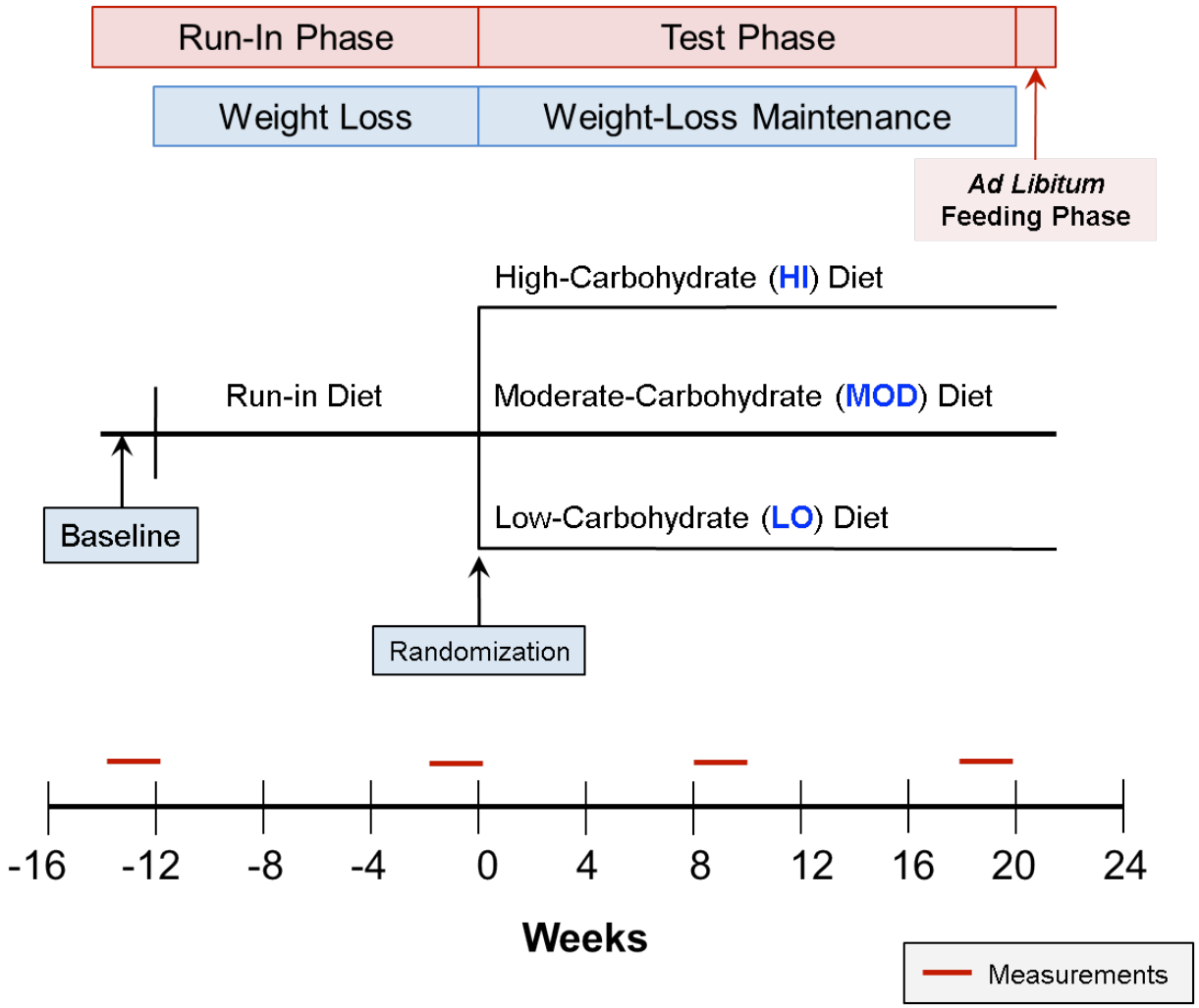
Specific Aim #4: To evaluate the effects of 3 diets varying widely in carbohydrate-to-fat ratio on voluntary food intake and body weight during an *ad libitum* feeding phase.

Hypothesis

4 Energy intake and body weight will differ among diets during the 2-week *ad libitum* feeding phase (implemented after the test phase of weight-loss maintenance).

Secondary outcomes: energy intake, body weight.

Figure 1. Study Design.



Study Timeline

	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun
Year 1 *(2013-2014)*												
Study Start-up												
Recruitment, Cohort 1								n=75				
Year 2 *(2014-2015)*												
Preparation, Cohort 1												
Implementation, Cohort 1												
Recruitment, Cohort 2								n=75				
Year 3 *(2015-2016)*												
Preparation, Cohort 2												
Implementation, Cohort 2												
Year 4 *(2016-2017)*												
Data Management and Analysis												

Inclusion and Exclusion Criteria

Inclusion criteria	**Exclusion criteria**
• Aged 18 to 55 years (students, faculty, staff). • BMI ≥ 25 kg/m^2. • BMI < 40 kg/m^2 and weight ≤ 300 lbs (136 kg). • Medical clearance from a primary care provider. • Plans to matriculate as a student at FSU or work on campus throughout the academic year of enrollment in the study. • Willingness to eat and drink only the foods and beverages on the study menus during participation, with no food allergies or aversions. • Willingness to eat in the dining hall. • Willingness to abstain from consuming alcohol during participation.	• Change in body weight exceeding ±10% during prior year. • Recent adherence to a special diet. • Recent adherence to a vigorous physical activity regimen (as indicated by participation in a varsity sport). • Chronic use of any medication or dietary supplement that could affect study outcomes. • Current smoking (1 cigarette in the last week). • Heavy baseline alcohol consumption (> 10 drinks/week) or history of binge drinking (≥ 5 drinks in 1 day, anytime in past 6 months). • Physician diagnosis of a major medical illness or eating disorder. • Abnormal laboratory screening tests (fasting blood glucose, TSH, CBC, BUN, Creatinine, ALT). • Plans for a "party" vacation during winter or spring break.
Additional exclusion criteria for females	
• Irregular menstrual cycles. • Any change in birth control medication during the 3 months prior to enrollment. • Pregnancy or lactation during the 12 months prior to enrollment.	

Dietary Energy and Macronutrient Composition

Dietary Variable	**Run-In Phase**	**Test Phase**		
	Energy Restriction	High (**HI**) Carbohydrate Diet	Moderate (**MOD**) Carbohydrate Diet	Low (**LO**) Carbohydrate Diet
Energy (% of weight maintenance needs)	60	100	100	100
Carbohydrate (% of total energy)	45	60	40	15
Fat (% of total energy)	30	20	40	65
Protein (% of total energy)	25	20	20	20