

**Title: Reduce “metabolic obesity” in the US**

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**Description of the problem:** Obesity is a global problem that undermines quality of life, increases risk of chronic disease, and incurs billions annually in healthcare costs. Obesity is a relatively recent problem, having reached epidemic proportions in the US within the past 50 years, concurrent with the change in food supply. As Americans were presented with, and chose to consume, increasingly processed food products, waistlines expanded and incident disease rates escalated for type 2 diabetes (T2D) and related metabolic diseases. Consuming processed food is analogous to injecting a drug intravenously; it is rapidly digested and absorbed, and has an effect on metabolism that is disproportionate to its energy content.

Despite the obvious connection between diet composition and obesity, Americans were advised not to shun processed food, but instead to count calories and exercise more. This strategy for promoting weight loss was a spectacular failure, creating frustration for both patient and practitioner. Negative energy imbalance (eating fewer calories than one requires) triggers a series of compensatory physiological adjustments to ensure homeostasis. Specifically, energy expenditure declines, metabolic efficiency increases, and appetite increases. As a result, intentional weight loss based on “counting calories” rarely succeeds at attaining long-term weight loss. In contrast, transitioning to a whole-foods (minimally processed) diet enables the system to equilibrate at a new, lower, set point that reflects endocrine adjustments that respond to diet composition. This new, lower, body weight is achieved in the absence of energy restriction or hunger. This common sense and physiology-based approach to weight loss is not commonly espoused by national health agencies because it is not intuitive, and because it would have a negative impact on certain industries. Thus, Americans continue to be told that they are overweight because they simply aren’t trying hard enough to lose weight. To solve the obesity epidemic, it is critical to provide Americans with accurate information both on the cause of unintended weight gain, and on practical and acceptable solutions to weight loss.

Although “weight loss” is the proximate aim, good health is the ultimate goal. It is often incorrectly assumed that somehow body fat “causes” disease. A more accurate model is that excess adipose tissue (“fat”) is a symptom of a diet that results in allocation of energy specifically to storage as fat. This diet also causes insulin resistance and inflammation, the root causes of metabolic disease. Thus, obesity and disease develop in parallel in response to a diet rich in added sugar and processed carbohydrates. Obesity is not the ideal marker for disease risk because its specificity is low; many “lean” individuals have poor metabolic health, and many “obese” individuals are healthy. Thus, effective screening tools are needed for identifying “metabolically obese” individuals across the body weight spectrum and targeting these individuals for intervention. Further, “weight loss” efforts should focus on metabolic health rather than scale weight. Primary to this goal is evaluation of insulin resistance and inflammation, two related processes that underlie the etiology of all chronic disease. The single most informative blood analyte is fasting insulin, which reflects insulin resistance, and can be detected years before elevated glucose and HbA1c. Shockingly, fasting insulin is rarely included in a physician’s laboratory panel, and point-of-care instruments do not exist for monitoring insulin. However, technology is available at UAB for development of such an instrument for real-time data collection and wireless connectivity with the hospital or service provider.

A second novel and informative metabolic measure is body geometry. Insulin resistance and inflammation contribute to the characteristic “apple” shape of the metabolically unhealthy patient. Dysfunctional, inflamed, adipose in the periphery fails to store excess lipid, resulting in “ectopic” adipose stores in the visceral space and organs. Thus, body geometry, deriving from either genetic or environmental (lifestyle) factors, can be used as a non-invasive surrogate for metabolic health and risk for disease. Body geometry can be objectively evaluated and tracked using new, automated, instrumentation based on infra-red light and digital reconstruction. It can also be evaluated using digital images, as might be obtained from a smart phone camera; such technology is available at UAB.

**Plan of work.** The ultimate plan is to develop a cost-effective method of evaluating metabolic health in adults and children across the nation using insulin, inflammation, genotype, and body geometry; prescribe a semi-personalized, affordable, diet prescription based on patient health status/risk level; monitor intervention progress using noninvasive markers; and monitor health status using insulin and inflammation. The project would be developed and pilot tested at UAB (phase 1), and then expanded to the city of Birmingham (phase 2) and eventually the United States (phase 3), leveraging ongoing collaboration with HEAL Alabama to address pediatric obesity, and using infrastructure developed at UAB for home healthcare testing across the US.

**Phase 1** would include development of a phone app for assessing body geometry, a point-of-care insulin analyzer, and a phone app for the nutrition intervention (including options for menu/recipe selection with price-point choices, and grocery delivery via partner companies); and piloting the intervention within UAB (Athletics, students, staff, faculty). UAB students would be trained to collect data and provide the intervention. Data collection would include body geometry by commercial instrument, markers of inflammation, laboratory insulin, noninvasive markers, and a genetic insulin resistance score. Major insurers would be invited to participate, and to cover the cost of insulin assessment. Data would be used both to develop a predictive algorithm for a high-risk patient, and to track progress with the intervention.

**Phase 2** would involve extending the intervention to the City of Birmingham, focusing on city employees, and school students. Mayor Woodfin would be involved with city employee outreach, and “HEAL Alabama” would provide the intervention to school children. This phase would incorporate the newly developed insulin analyzer and body geometry phone app.

**Phase 3** would sample individuals across the US and provide the intervention via remote technology, leveraging the infrastructure already in place at UAB for the REGARDS (Reasons for Geographic and Racial Differences in Stroke) study. Individuals at excess risk at all sites would be identified during follow-up and targeted for more intensive healthcare treatment.

**Desired outcomes:** 1) Measurement of insulin, body geometry, inflammation, and genotype will allow identification of participants who are at elevated risk for chronic disease that is more accurate than current “obesity” cut-points based on body mass index (BMI). 2) Real-time monitoring of insulin and periodic monitoring of noninvasive markers will provide feedback to participants that motivates them to adhere to the intervention, and provides the study team with information on participant progress that is useful for identifying individuals whom require additional contact from the study team. 3) The remote intervention will promote loss of central body fat and improvement in metabolic health; the lifestyle change will be acceptable to participants and sustainable. 4) The intervention will be effective within all socioeconomic sectors.

## **Team Members:**

### UAB Nutrition Sciences:

Barbara A. Gower, PhD, Professor

W. Timothy Garvey, MD, Professor

Amy M. Goss, PhD, RD, Assistant Professor

Role: Study oversight; nutrition intervention development and implementation.

### UAB Psychiatry:

Aaron Fobian, PhD, Assistant Professor

Role: Pediatric intervention development and implementation; collaboration with Christy Swaid and HEAL Alabama.

### UAB Epidemiology:

Olivia Affuso, PhD, Associate Professor, PI R01HL107916, “A photographic method for human body composition assessment.”

Role: Development of a phone app for body geometry.

### UAB Biostatistics:

Suzanne Judd, PhD, Associate Professor, Director of Study Operations for REGARDS.

Role: Development and implementation of national home health care based screening and testing; implementation of the remote nutrition intervention at the national level.

### UAB Electrical & Computer Engineering:

Mohammad R. Haider, PhD, Associate Professor, Director of Analog Electronics Laboratory, Director of Bioinspired Integrated Circuit (BIC) Design Laboratory.

Role: Development of a point-of-care insulin analyzer with phone app based encrypted communication.

### Georgia State University:

Dora Il'yasova, PhD, Associate Professor

Role: Development of urine F2-isoprostanes (F2I) as a noninvasive monitoring tool. F2I are a bi-product of fat oxidation, and are higher in individuals who are burning fat and losing weight. Low F2I are also a risk factor for T2D. Drs. Gower and Il'yasova will collaborate to develop and test the use of F2I as a marker for both a successful diet intervention and as a risk factor for T2D.

### HEAL Alabama:

Christy Swaid

Role: Implementation of the pediatric intervention through HEAL Alabama, an outreach organization with over 85 Alabama elementary schools.

### Future partners:

Blue Cross / Blue Shield of Alabama

Shipt grocery delivery service