



NIH Obesity Research Task Force



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Co-chairs of the NIH Obesity
Research Task Force
November 20, 2008

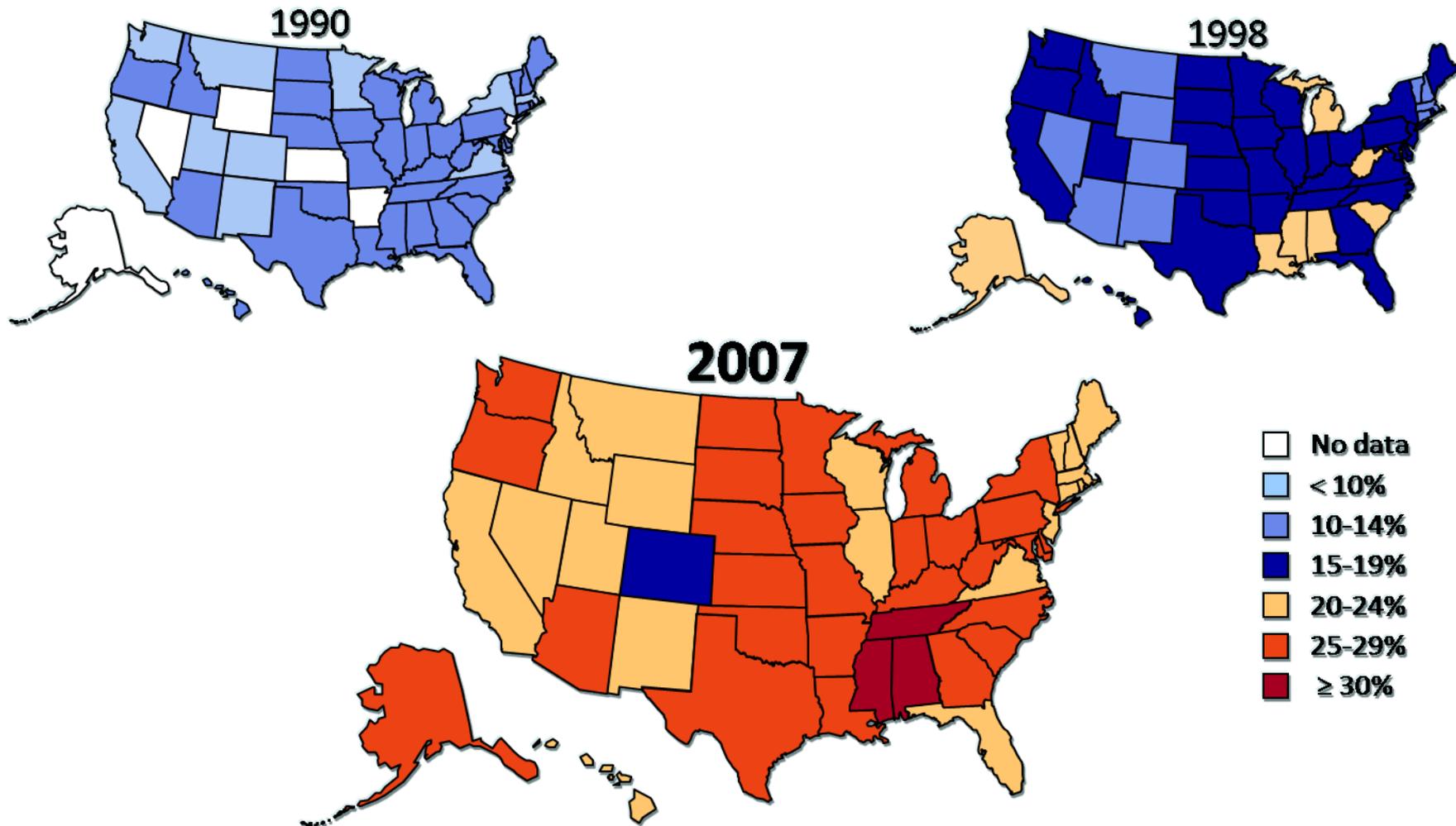


Overview

- Prevalence of Obesity in the U.S. and Health Consequences
- NIH Obesity Research Task Force (ORTF)
- Trans-NIH Obesity Efforts Fostered or Enhanced by the ORTF
 - Identifying factors that cause/contribute to obesity
 - Enabling measurement and analysis of diet, physical activity, and other contributors to obesity
 - Developing, testing, and evaluating intervention strategies
 - Disseminating research results to healthcare professionals, patients, and the public
- Summary

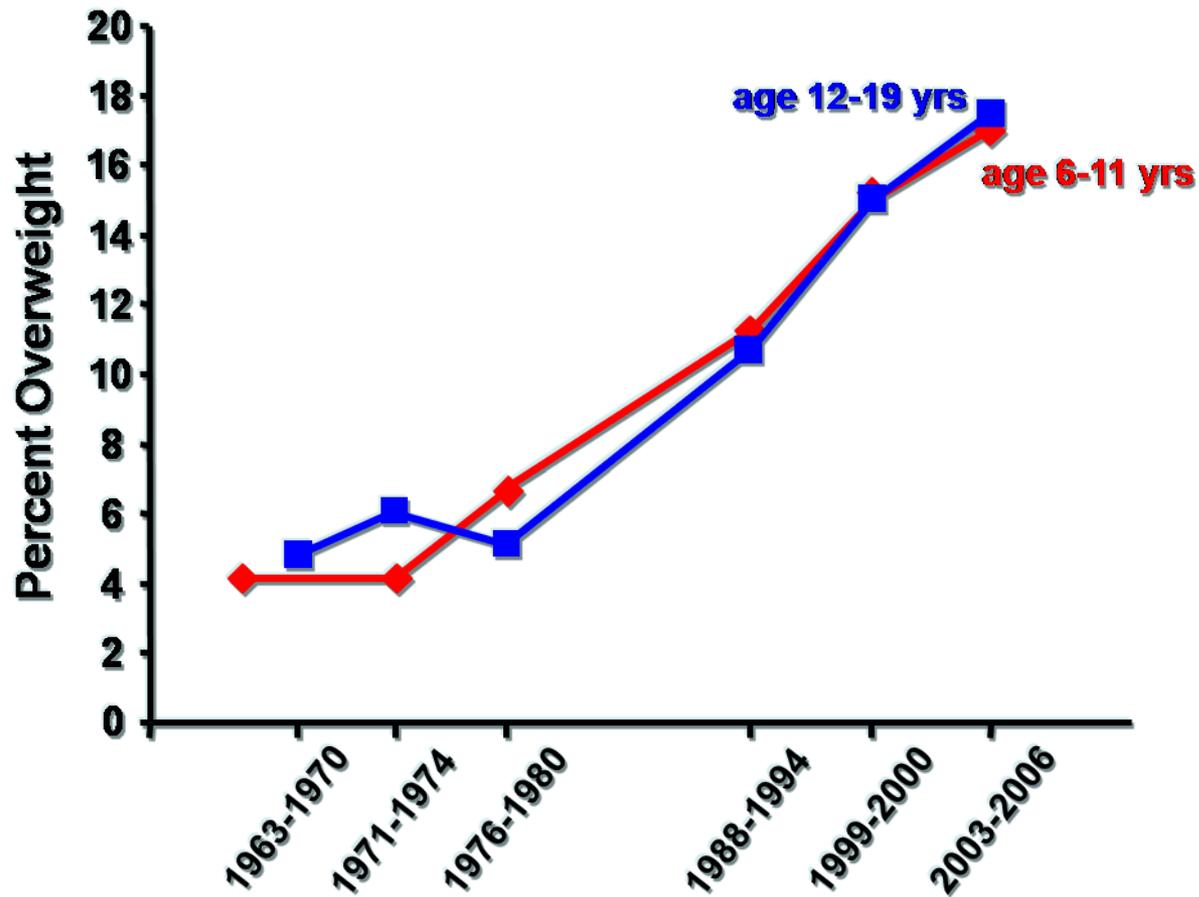
Obesity Trends* Among U.S. Adults, BRFSS, 1990, 1998

(*BMI ≥ 30 , or about 30 lbs. overweight for 5'4" person)



Source: Behavioral Risk Factor Surveillance System, CDC

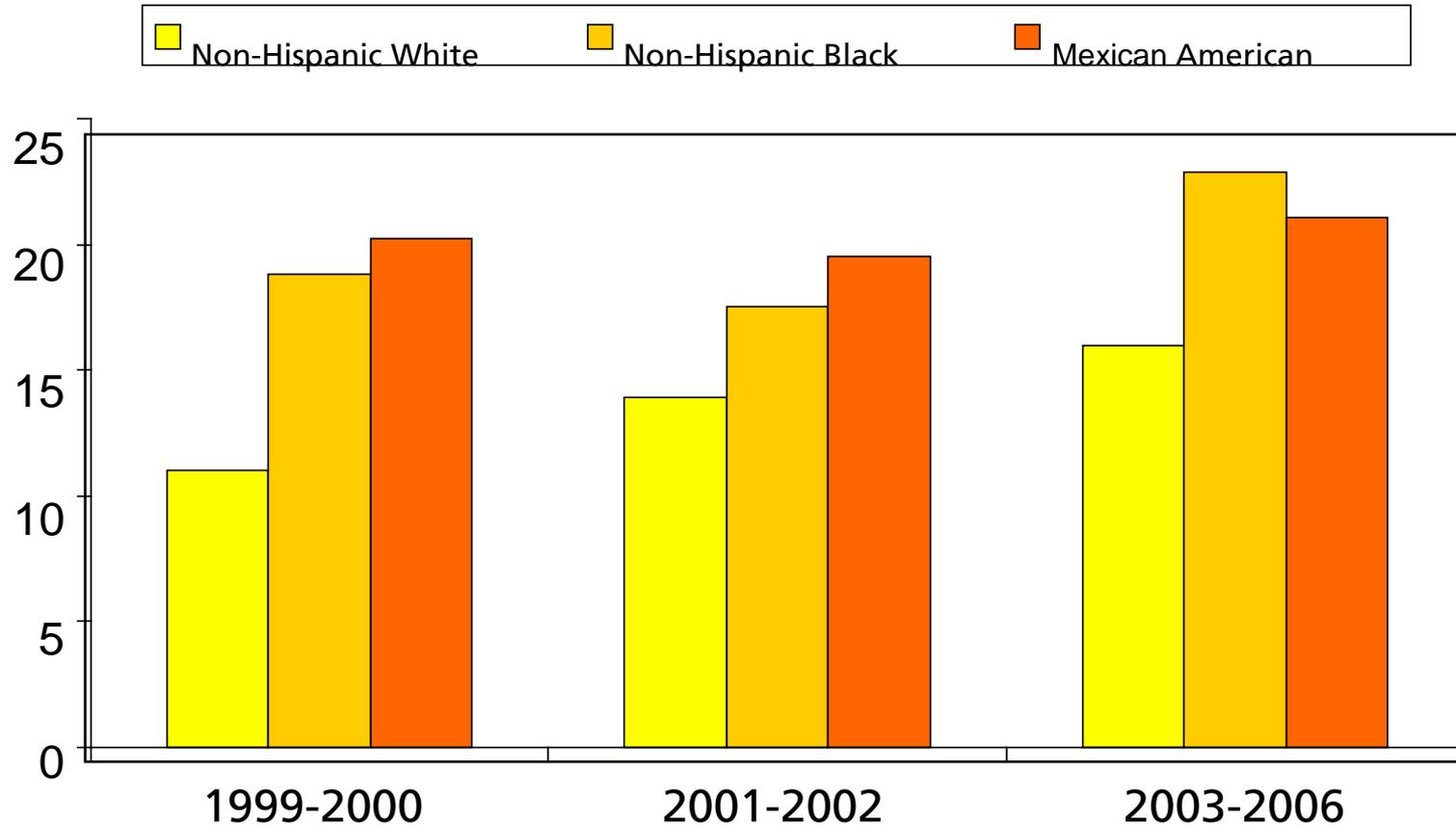
Childhood Obesity* Trends



*BMI \geq 95th percentile of BMI-for-age, 2000 CDC growth charts

SOURCES: NHES II & III, NHANES I, II, & III, NHANES 1999-2004; Ogden et al. *JAMA* 2002, *JAMA* 2006, *JAMA* 2008

Health Disparities: Prevalence of Overweight/Obesity in U.S., Ages 12-19 Years, by Race-ethnicity



Ogden CL et al, JAMA 2006, 295:1549-55; JAMA 2008, 299:2401-5

Obesity is Relevant to the Missions of Many NIH Components

Medical Complications of Obesity:

Pulmonary disease

- abnormal function
- obstructive sleep apnea
- hypoventilation syndrome

Pancreatitis

Nonalcoholic fatty liver disease

- steatosis
- steatohepatitis
- cirrhosis

Gall bladder disease

Cancer

breast, uterus, cervix, prostate, kidney
colon, esophagus, pancreas, liver

Skin

Gout

Stroke

Idiopathic intracranial hypertension

Cataracts

Coronary heart disease

Diabetes

Dyslipidemia

Hypertension

Gynecologic abnormalities

- abnormal menses
- infertility
- polycystic ovarian syndrome

Osteoarthritis

Phlebitis

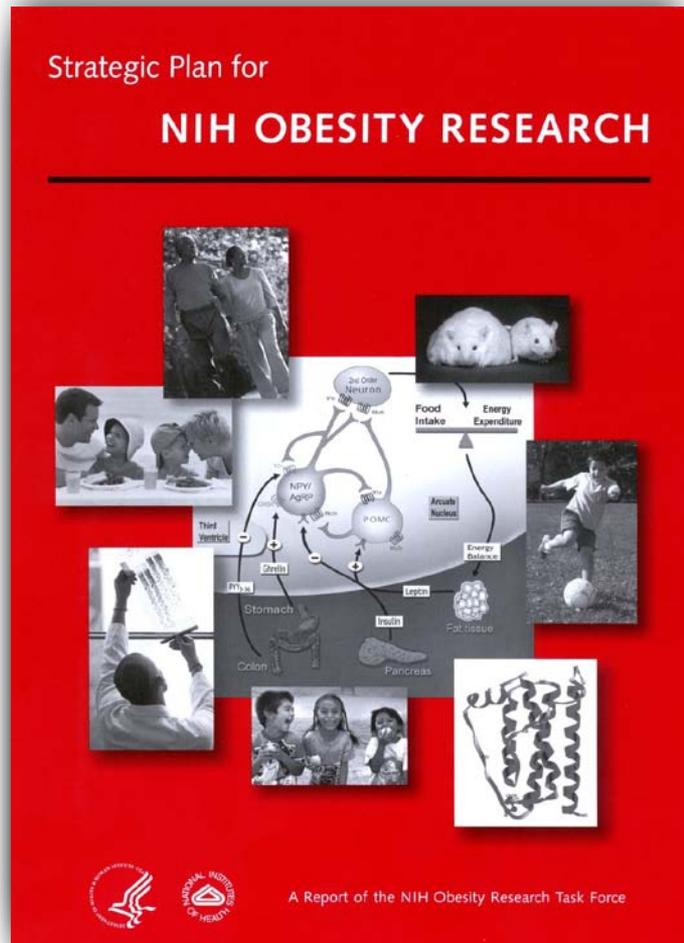
- venous stasis



NIH Obesity Research Task Force



Strategic Plan for NIH Obesity Research (2004)



Basic science

Clinical investigations

Epidemiologic studies

Behavioral and environmental studies

Economic research

Translational research projects

Education and outreach programs

FY 2007 NIH Funding for Obesity Research: \$661 million

<http://obesityresearch.nih.gov>

Updating the Strategic Plan

Purpose of the *Strategic Plan for NIH Obesity Research*

Serves as a guide for:

- Coordinating research activities across the NIH
- Enhancing the development of new efforts based on identification of areas of greatest scientific opportunity and challenge.

Updating the Strategic Plan

Published in 2004, the *Strategic Plan* was intended to be updated as research progressed and new opportunities arose.

- Given the rapidly advancing state of science, an update is timely.
- NIH staff recently began an effort to develop an updated strategic plan. We will solicit input from external investigators, voluntary and professional organizations, health care professionals, and the broader public.

NIH ORTF – Research Efforts

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Obesity and Intrauterine Environment

Workshop: The Intrauterine Environment: Long-term consequences for obesity and metabolic disease
September 2005

Funding Opportunity Announcement – FY 2005-06
NIDDK, NHLBI, NCI

- Studies funded: animal and human

Intrauterine Environment Investigators meeting and workshop: November 2007

- Workshop focused on clinical/preclinical research

Obesity and the Intrauterine Environment

Examples of Ongoing Studies

- Effects, in rodent model, of high fat diet-induced maternal obesity on offspring – potential metabolic alterations, epigenetic modifications
- Effect of maternal diabetes on offspring's risk for damage to pancreatic beta cells and type 2 diabetes, in rodents; published finding of impaired insulin secretion in offspring *Am J Phys Endo Metab*, 2007
- Influence of obesity during pregnancy on offspring's body weight, glucose levels, and feeding behavior, in non-human primate model.
- Impact of maternal diet, in rodents, on offspring's sympathetic nervous system development, and resulting effects on pancreatic function and fat tissue.
- Effects of maternal high fat diet, in primates; recent finding of changes in epigenetic marks in offspring and association with liver abnormalities in offspring similar to fatty liver disease *J Mol Endo*, 2008.
- Possible mechanisms underlying associations among maternal obesity, high birth weight, and later breast cancer in offspring

Research on the Economics of Diet, Activity, and Energy Balance

Funding Opportunity Announcements (FY2005 – present, active)

NCI, NIDDK, NIA, NHLBI, OBSSR, NINR

- To foster trans-disciplinary obesity research that integrates economics
- Target NEW group of researchers with expertise and experience in health economics and health services research
- Foster collaboration between researchers from these and more traditional disciplines of cancer and other chronic diseases

Research on the Economics of Diet, Activity, Energy Balance

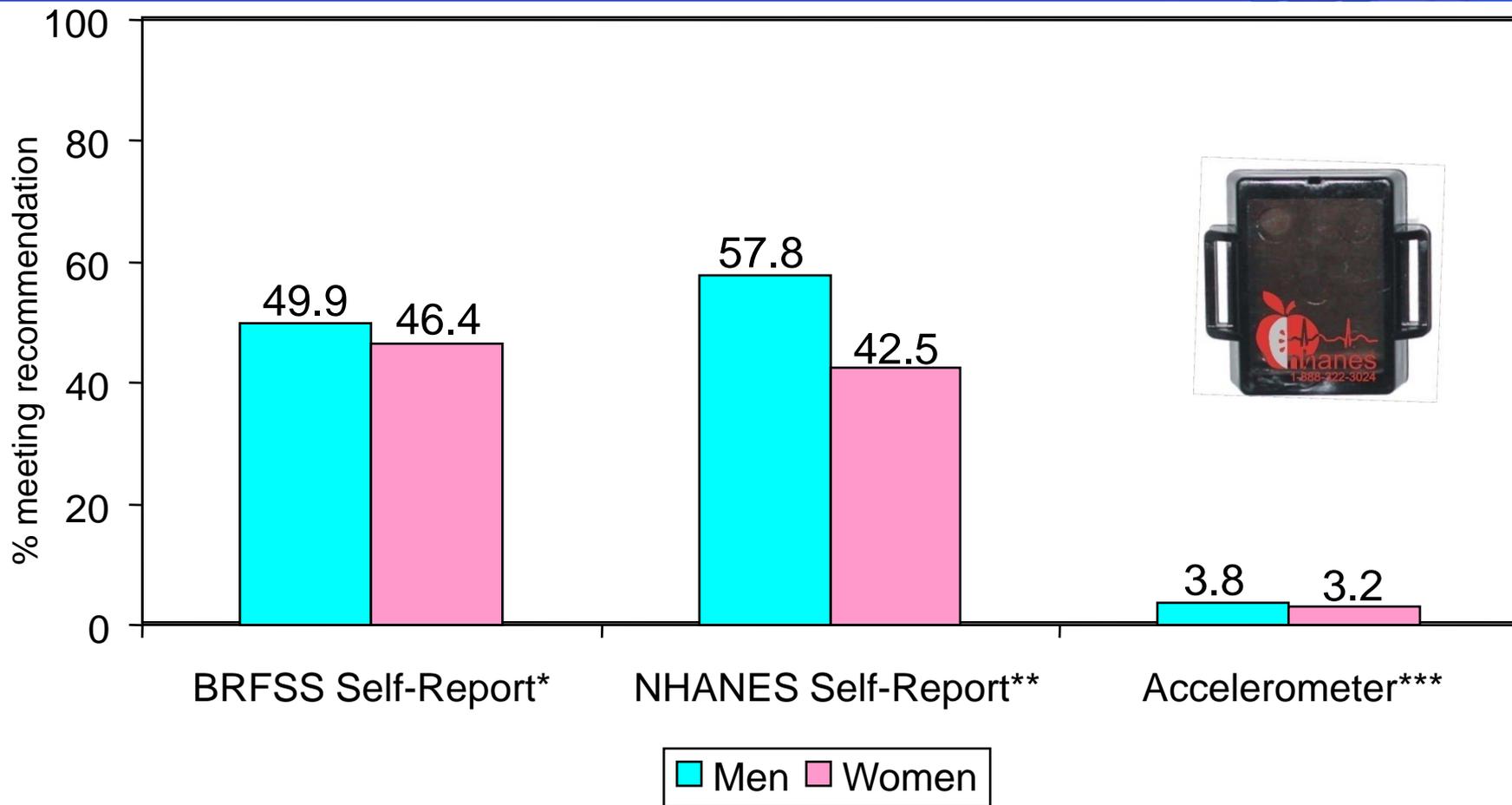
Example of Study: Cost-effectiveness in Physical Activity Promotion

Overview of Cost-Effectiveness Results for Physical Activity

Type of intervention (# of studies)	Costs per person	MET hours gained per day	C/E ratio (\$ per MET hour gained)
Point of decision reminders to be active (12)	\$0.15 (\$0 ~ \$1.34)	0.004/day	0.56 (0.00 ~ 4.72)
Community campaign (2)	\$14.93; \$0.46	0.001, 0.16	1.50, 0.01
Individually-focused behavior change (28)	\$84.82 (\$0.59 ~ \$621)	0.76	1.55 (0.01 ~ 35.8)
Social support (12)	\$566 (\$5 ~ 4305)	1.09	5.89 (0.07 ~ 60.2)
School-based PE (19)	\$78.36 (\$0.00 ~ \$538)	0.64	3.01 (0.00 ~ 39.3)
Environmental & policy approaches (3)	\$15.08; \$5.07; \$137.46	1.71; 2.03; 0.79	0.40; 0.17; 4.47

*MET = Metabolic Equivalent = energy expended at rest

Percentage of U.S. Adults Meeting Physical Activity Recommendations



*BRFSS 2005 (30 min x 5d mod or 20 min x 3 d vig)

** NHANES 2003-2004 (150 min/week)

*** NHANES 2003-2004, 20-59 y (Troiano et al., MSSE 2008, 40:181-188) 30 min x 5d mod or greater

Geographic and Contextual Influences on Energy Balance-Related Health Behaviors

New Funding Opportunity Announcement, 2008 (active)
NCI, NHLBI, NINR, NICHD, OBSSR

- "...to encourage grant applications that propose hypothesis-driven projects exploring **associations between the built environment**, other contextual features of where people of all ages live and work, **and health behaviors related to energy balance.**"
- Generation and addition of new geographic information system (GIS) data layers
- Analyses of existing confidential geographic-based data
- Merging multiple health-related data resources to allow new analyses

Obesity and Other Metabolic Side-effects of Psychotropic Medications

MENTAL ILLNESS

- Schizophrenia
- Schizo-Affective
- Bipolar
- Depression etc.

PSYCHOACTIVE DRUGS

- Antipsychotics (Mostly SGA)
- Mood Stabilizers
- Antidepressants



Illness & Lifestyle Factors

Medication Effects

- Obesity
- Type 2 Diabetes Mellitus
- Dyslipidemia
- Increased CHD Morbidity and Mortality

METABOLIC DISTURBANCE

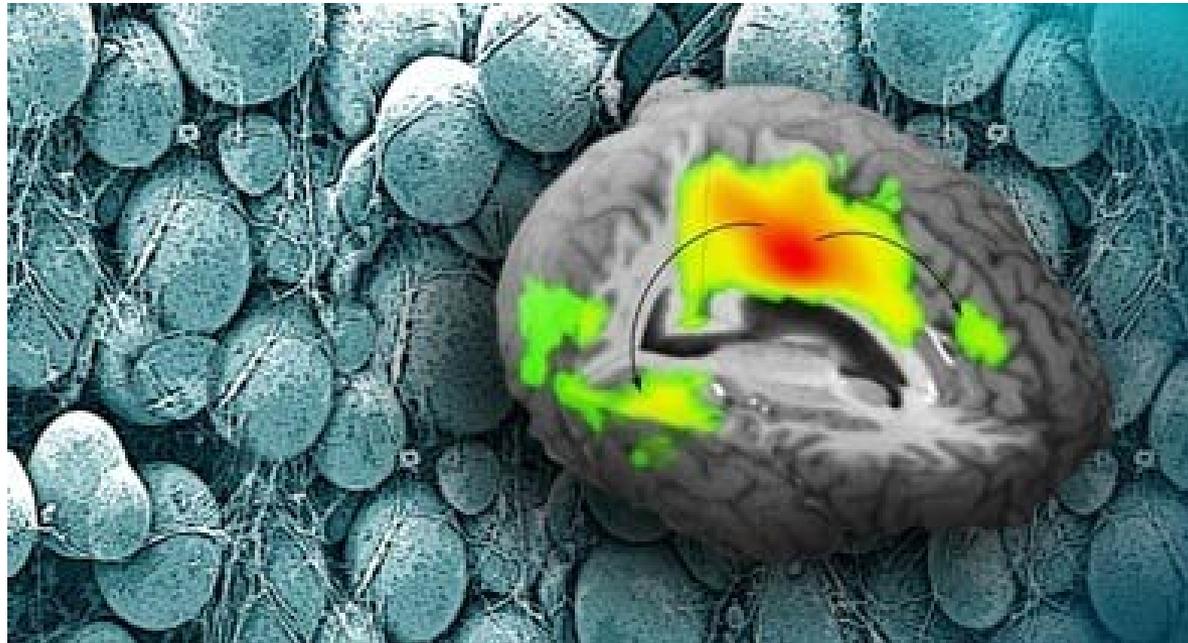
Adverse Metabolic Side Effects of Second Generation Psychotropic Medications Leading to Obesity and Increased Diabetes Risk

New Funding Opportunity Announcement (FY 2008, active)
NIDDK, NIMH

To encourage research to examine the adverse metabolic effects of psychotropic medications in animals and humans:

- Increase the understanding of the nature, rates, and pathophysiology of adverse metabolic effects of psychotropic medications
- Elucidate biomedical and psychosocial risk factors for the development of metabolic adverse effects of psychiatric therapeutics
- Develop interventions to prevent and/or mitigate metabolic adverse effects across the lifespan

Neuroimaging in Obesity Research



- Workshop – October 2008 *NIDDK, NIDA, NIA, NIMH, NIBIB, NCCAM, OBSSR*
- New Funding Opportunity Announcement (FY 2008, active)
NIDDK, NIDA, NIBIB

Solicits studies using neuroimaging approaches in animals and humans to study the many interacting roles of the brain in obesity and its pathogenesis and complications.

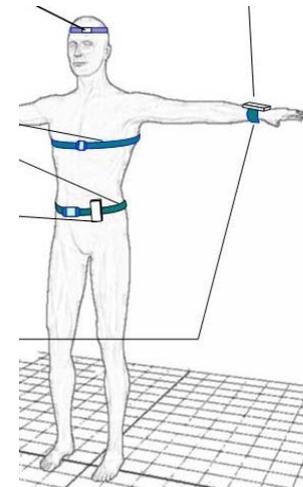
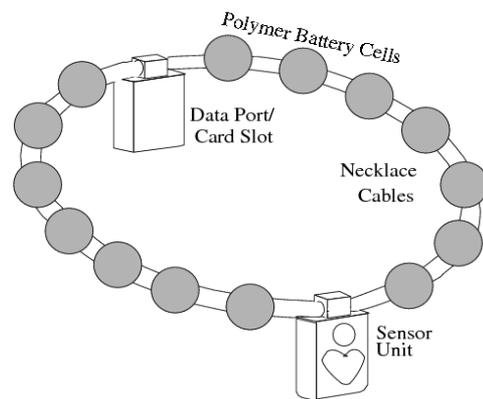
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Improved Measures of Diet and Physical Activity for the Genes and Environment Initiative (GEI)

Funding Opportunity Announcement (FY 2007)
NCI, NHLBI

- Goal: To develop innovative technologies to measure diet, physical activity, or both
- Projects funded address measures of diet, physical activity, both
- Two projects highlighted here (Drs. Carol Boushey and Stephen Intille)



GEI: Technology Assisted Dietary Assessment

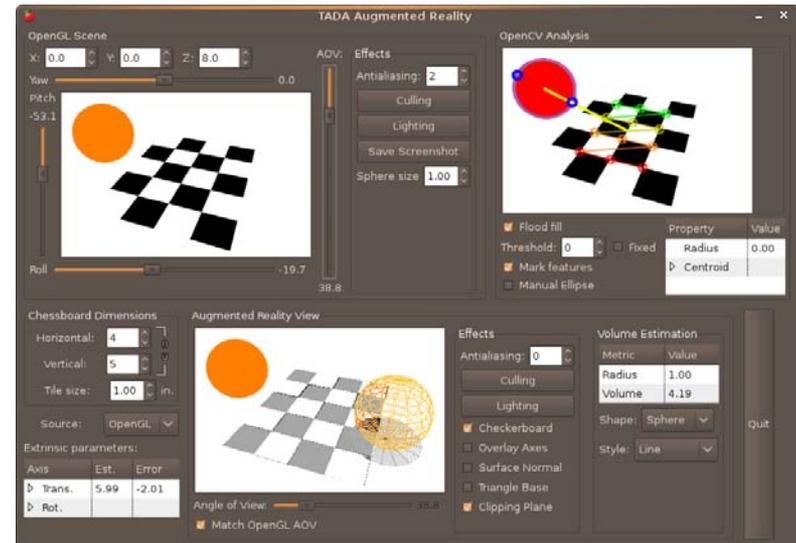
Carol Boushey, Purdue University



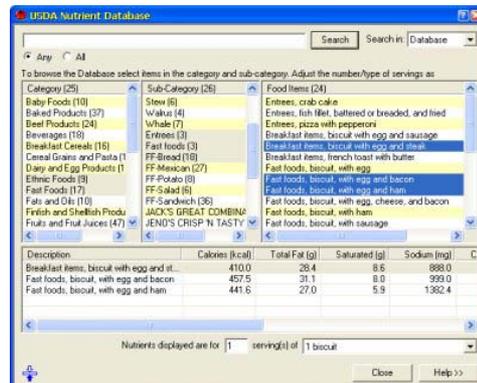
1. Photos are taken with mobile phone before and after foods consumed



2. Photos may be tagged with additional details as needed



3. Image segmentation, analysis, and processing occurs



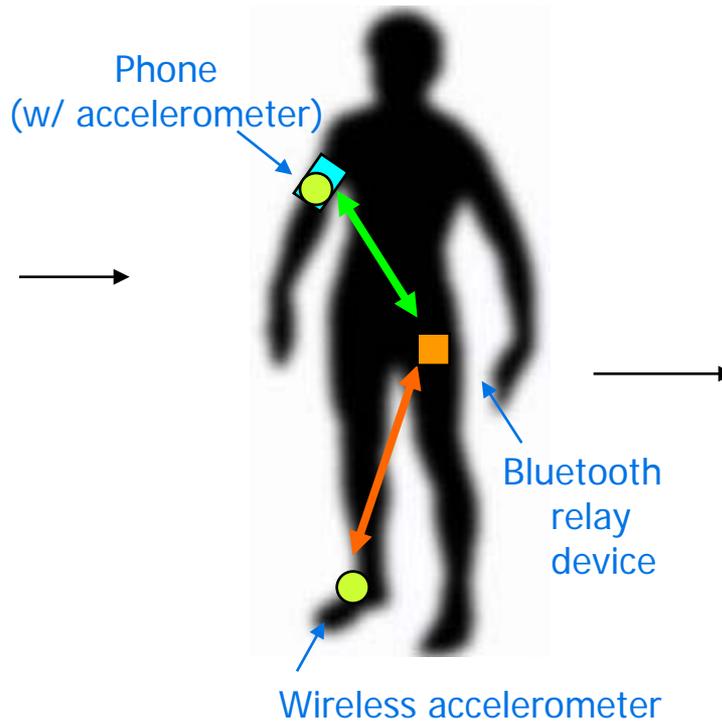
4. Data links to nutrient database for fully automated assessment

GEI: Population-Scale Physical Activity Measurement

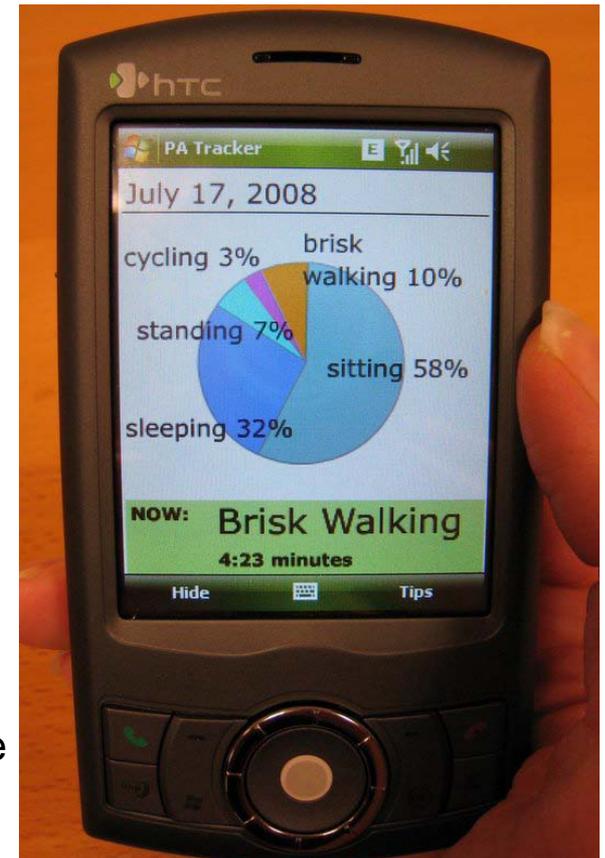
Stephen Intille, MIT



1. Design allows flexibility and low-participant burden



2. Two+ miniaturized sensors communicate with mobile phone via Bluetooth



3. Physical activity output collected in real-time

Improving Diet and Physical Activity Assessment

Ongoing Funding Opportunity Announcements

NCI, NHLBI, NIA, NICHD, NIDDK, NIMH, NINR, ODS

Examples of ongoing funded studies:

- Developing Measures of the Built Nutritional Environment
- Heart Rate and Movement Integration to Improve Physical Activity Assessment
- Validation of System for Observing Play and Recreation in Communities (SOPARC) and Use in Diverse Populations
- Development of a Tool to Measure Food Availability in the Home
- Physical Activity Assessment Using Variability in Accelerometer Counts
- Novel Analytic Techniques to Assess Physical Activity
- Nutrition and Physical Activity Assessment Study in the Women's Health Initiative (WHI) (broad range of biomarkers and of frequencies, records, and recalls for both nutrition and physical activity)

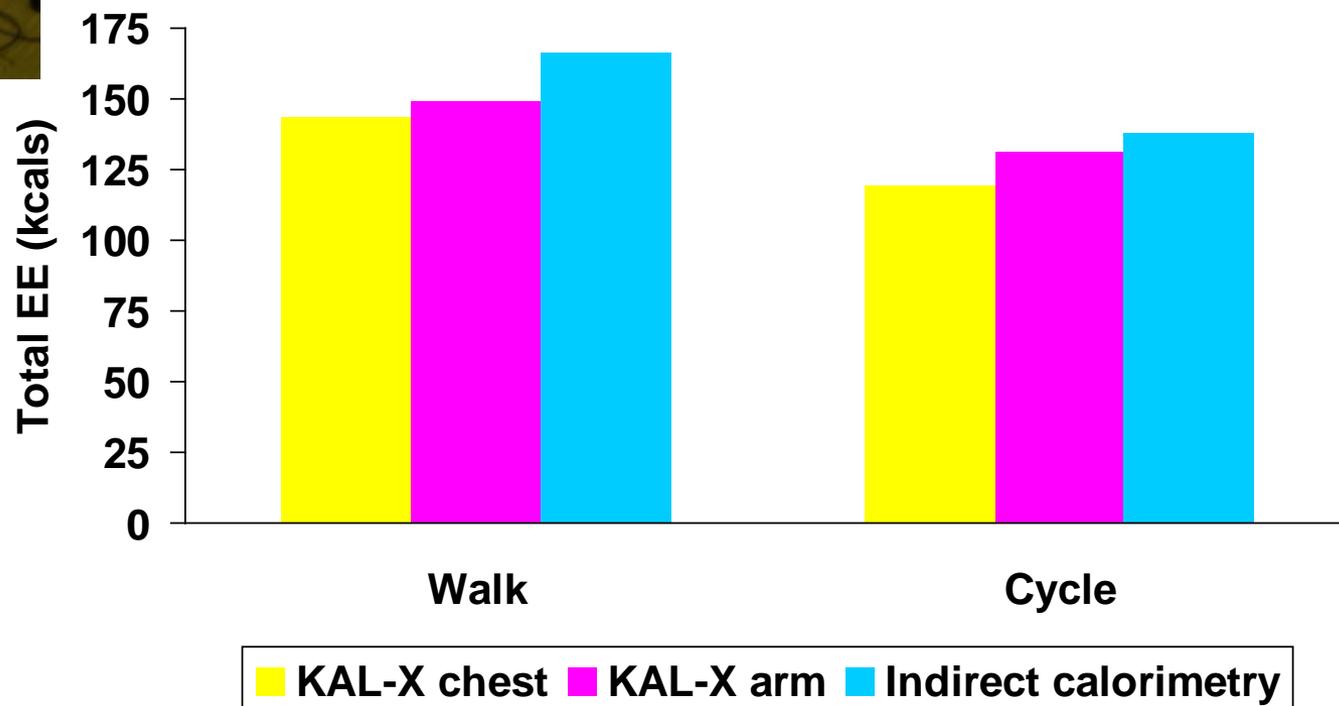
Improving Diet and Physical Activity Assessment

Example of study: KAL-X Sensor



KAL-X Sensor

Comparison of corrected energy expenditure (KAL-X) with measure energy expenditure.



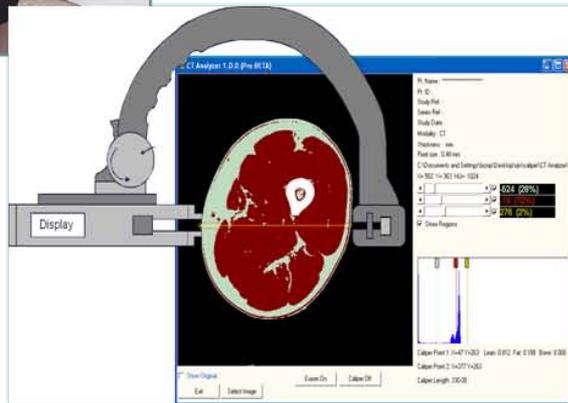
Bioengineering Approaches to Energy Balance and Obesity

Five Funding Opportunity Announcements – FY 2005, FY 2006, FY 2007

NHLBI, NIA, NCI, NIBIB, NIDDK; one announcement co-funded by National Science Foundation

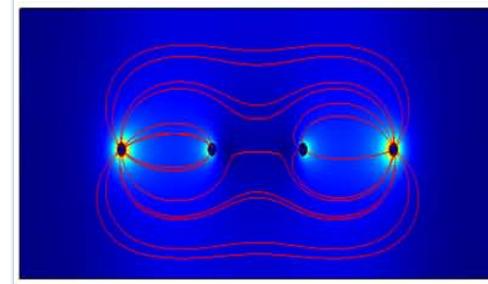
Examples of funded studies

Monitoring Sarcopenic Obesity in the Elderly

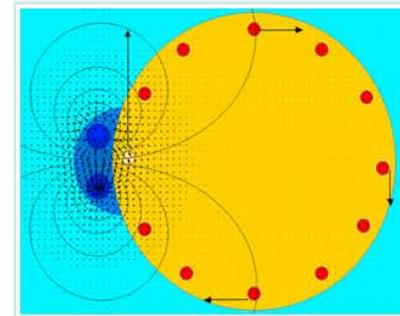


Joseph Kehayias, Tufts University

Noninvasive Sensors of Metabolic Activity



Electric field distribution in vicinity of electrodes, used to probe electromagnetic responses of live cells.



Electric field driven torque model of ATP synthase, showing stator (a-subunit, blue) and c-ring (orange).

John H. Miller, Jr., University of Houston

Innovative Statistical and Computational Methodologies for Design and Analysis of Multilevel Studies on Childhood Obesity

New Funding Opportunity Announcement (FY 2008)

NICHD, NHLBI, OBSSR

- Building block of a multilevel obesity research framework
- To form teams of pediatric obesity experts and computational methodologists; useful for future multilevel research efforts
- Focuses on methodology development and application
- Requires use of simulated and/or secondary data
- Examples of studies that would be of interest: agent-based models, system dynamics models, integration of macro and micro simulations, Bayesian statistics for quantification of complex system pathways

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Site Specific Approaches for the Prevention or Management of Pediatric Obesity

Funding Opportunity Announcement (FY 2005)
NIDDK, NCI, NICHD, OBSSR, ODP



The studies encompass a variety of sites and diverse populations:

- **Various Settings:** Head Start centers, home, schools/after school, urban and rural, internet, community
- **Different Target Populations:** infants, children, adolescents; low-income; diverse race/ethnicity

Examples of funded studies:

- Child Health Initiative for Lifelong Eating and Exercise (CHILE): 3-5 yrs, rural Hispanic and American Indian children – Head Start Centers, homes, communities
- Obesity Prevention and Control at Community Recreation Centers: 7-9 yrs, urban neighborhoods–community recreation centers, homes
- Reducing Sugar-Sweetened Beverage Consumption in Overweight Adolescents: high school students in urban schools – homes, schools



Prevention and Treatment of Pediatric Obesity in the Primary Care Setting

Funding Opportunity Announcement (FY 2004)

NICHD, NHLBI, NINR, NIDDK, NIDCR, OBSSR, ODP

- Majority of studies target obesity in younger children; a few are in adolescents and youth with BMI > 95th percentile.

Examples of Studies Funded

- Changing maternal diet to affect toddlers' diet
- Feasibility of healthy weight intervention in dental care setting
- Use of nurse practitioners in chronic care model to focus on TV and diet; 2-6-yr-olds across 10 clinics
- Multi-component behavior modification in overweight adolescents 12-17 y

Look AHEAD (*Action for Health in Diabetes*)

NIDDK, NHLBI, NINR, NCMHD, ORWH, and CDC

Objective: Multi-center clinical trial to examine the long-term effects of an intensive lifestyle intervention designed to achieve and maintain weight loss versus a diabetes support and education program in overweight/obese persons with type 2 diabetes

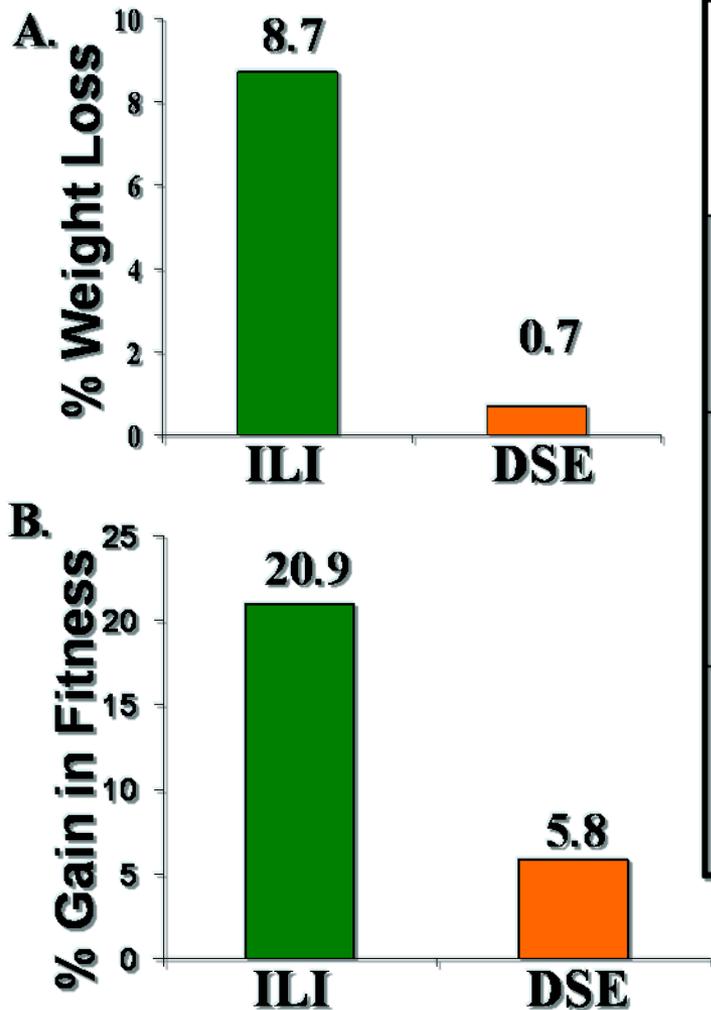
Enrollment Completed:

5145 overweight/obese adults (BMI = 36 kg/m²)

Average age: ~59 years; 37% minority population

Primary Outcome: Incidence of CVD morbidity and mortality over 11.5 yr. period

Look AHEAD - Results-1 Year



	Intensive Lifestyle Intervention	Diabetes Support & Education (control)	P-value
HbA1c (%), Baseline	7.25	7.29	0.26
HbA1c (%), Year 1	6.61	7.15	<0.001
Year 1 – Baseline	-0.64	-0.14	<0.001
Glucose (mg/dl), BL	151.9	153.6	0.21
Glucose (mg/dl), Y1	130.4	146.4	<0.001
Year 1 – Baseline (Fasting)	-21.5	-7.2	<0.001
Diabetes Med., BL	86.5%	86.5%	0.93
Diabetes Meds., Y1	78.6%	88.7%	<0.001
Y1 – Baseline	-7.8%	2.2%	<0.001

• **Future plans:** continue lifestyle intervention and outcomes collection

• **Follow-up:** 11.5 years

ILI=Intensive Lifestyle Intervention
DSE=Diabetes Support and Education.

Diabetes Prevention Program Outcomes Study (DPPOS)

NIDDK, NHLBI, NIA, NEI, NICHD, ORWH; and CDC, IHS



DPP multi-center clinical trial

- Demonstrated that type 2 diabetes onset can be prevented or delayed in adults at high risk, with lifestyle intervention or drug metformin
- Study population - Ethnically diverse, overweight/obese adults with pre-diabetes
- Lifestyle intervention - Goal of modest weight loss achieved through moderate exercise and reduced dietary fat and calories.
- Dramatic results - Lifestyle intervention: 58% reduction in diabetes; Metformin: 31% reduction

DPPOS

- Ongoing follow-up study to examine durability of DPP interventions in preventing or delaying diabetes and its long-term complications (retinopathy, nephropathy, neuropathy, and cardiovascular disease)
-

Ancillary Studies to Major Clinical Research Studies

Leveraging investments in major clinical studies

- Ancillary Studies to Obesity-Related Clinical Trials
FY 2004-05 Funding Opportunity Announcement
(*NIDDK, NHLBI, NIA*)
- Current FOA (active): Ancillary Studies to Major Ongoing
NIDDK and NHLBI Clinical Research Studies (*NIDDK, NHLBI*)
 - Encourages investigator-initiated ancillary studies to ongoing large-scale clinical trials, epidemiological studies and disease databases supported by NIDDK or NHLBI
 - Focused on wide range of diseases and conditions including obesity; diabetes; acute and chronic liver disease; heart, lung, blood, and sleep disorders; chronic kidney disease; etc.

Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS)

- Funded in response to Ancillary Studies solicitation – ancillary to Longitudinal Assessment of Bariatric Surgery (LABS) for adults.
- **Observational study** of adolescent bariatric surgery at 5 pediatric centers.
- Goal - to enroll all adolescents scheduled for bariatric surgery at participating centers.
- Purpose - to assess short (30 day) and longer (2 yr) safety and efficacy of bariatric surgery in adolescents using standard data collection at all centers.
- Relationship of pre-op characteristics to post-op clinical outcomes and quality of life will be evaluated.
- Two ancillary studies to Teen-LABS have been funded, focusing on pre- and post-op psychosocial features and eating behavior.

The Trans-NIH Metabolic Clinical Research Unit

Established 2007

- **Mission:** To provide specialized, state-of-the-art facilities for comprehensive and collaborative research on factors driving the obesity epidemic.
- **Core Components:**
 - A comprehensive research team
 - 10-bed Inpatient Unit and a Phenotyping Unit
 - Metabolic Research Core
 - Mass Spectrometry Core
 - Hormone Assay Core
 - Imaging Core

Body composition lab



3 room calorimeters



Exercise testing lab



10-bed Inpatient Unit



Resting Metabolic Rate



Ad-lib vending machine



Large patient rooms



Elucidating Biologic Factors that Regulate Body Weight: Example of a Genetics and Translational Research Study

Identification of Brain Derived Neurotropic Factor (*BDNF*) as important in body weight regulation in humans

Observation in mice:

Mice with heterozygous deletion of *BDNF* gene: hyperphagia and obesity

EMBO J 19, 1290–1300, 2000)



Clues from WAGR Syndrome in Humans:

Wilms' Tumor

Aniridia

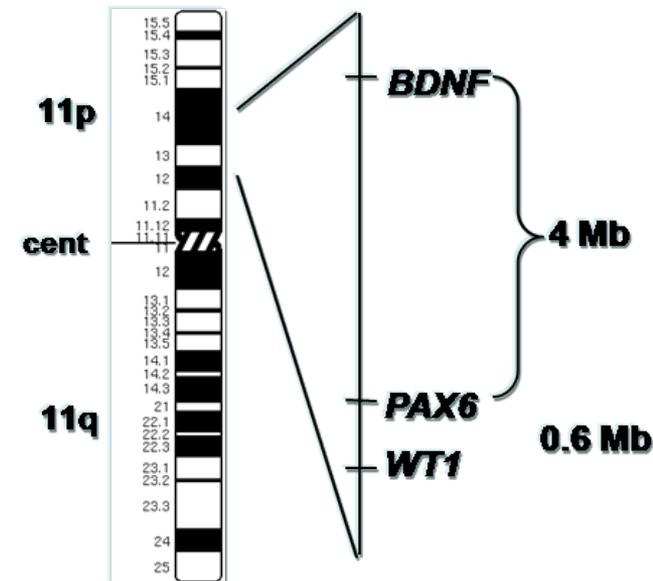
Genitourinary anomalies

Mental Retardation

Childhood-onset obesity in ~50%

Caused by heterozygous contiguous gene deletions in chromosome 11p13

BDNF is close to the WAGR Syndrome critical region



Trans-NIH Intramural Research: Collaborative Investigation of WAGR Syndrome

NICHD, NHGRI, NIDA

Hypothesis: Is obesity in WAGR syndrome due to heterozygous deletions of *BDNF*? (*half the normal gene copy number - haploinsufficiency*)

Study of 33 individuals with WAGR syndrome

- Anthropometric and clinical data
- Hyperphagia questionnaire (*Obesity 15:1816-26, 2007*)
- Region of chromosomal deletion determined: *BDNF* deleted in ~half of the patients
- Serum BDNF concentration assessed

Results

BDNF haploinsufficiency in people with WAGR Syndrome associated with:

- Greater BMI Z-score during childhood
- Higher prevalence of childhood overweight
- Greater reported hyperphagia
- Lower mean serum BDNF concentration

Conclude: These data provide strong evidence that BDNF is important in body weight regulation in humans

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National Survey of Energy Balance Related Care among Primary Care Physicians

Purpose: Obtain national data on physicians' knowledge, attitudes, and practices related to diet, physical activity and weight control (*NCI, NICHD, NIDDK, OBSSR, CDC, NHLBI, AHRQ*)

- **Physician factors:**
 - Clinical practice behaviors
 - Personal diet and exercise behaviors
 - Knowledge of the science and available guidelines
 - Attitudes, self-efficacy and importance of diet, physical activity and weight control in disease prevention
- **Practice-based/system factors:**
 - Organization of practice
 - Policy and information system supports
 - Availability and adequacy of reimbursement and billing practices
 - Supply of community resources for referrals

Survey Design

Sampling Frame – AMA Masterfile

- Primary Care Physicians (PCPs) providing patient care ≥ 20 hours/week

Nationally representative sample of PCPs Including:

- Physicians serving adults (Family Practitioners, Internists, Ob/Gyns)
- Physicians serving children (Family Practitioners, Pediatricians)

Sample Stratification

- Physician specialty
- Child vs. Adult patients
- Census region

Two survey questionnaires

- **Physician Questionnaire:** Knowledge, Attitudes and Behaviors to be completed by Physician
- **Administrator Questionnaire:** Practice and Systems Factors to be completed by Physician or Proxy (e.g. administrator, office manager, physician assistant, nurse)

Target is 4000 completed questionnaires; survey is ongoing

Evidence-Based Clinical Guidelines on Obesity for Adults: Steps in Update Process

NHLBI, NIDDK

1998



2008-2009

- Clinical Guidelines Leadership Group appointed
- Expert Panel identified
- Obesity evidence model developed
- Questions of interest identified
- Literature reviewed to identify evidence
- Level of evidence determined
- Draft Guideline developed
- Anticipated release: Spring 2010

We Can!TM An Evidence –Based Program to Help Children and Families Maintain a Healthy Weight!

NHLBI, NIDDK, NICHD, NCI



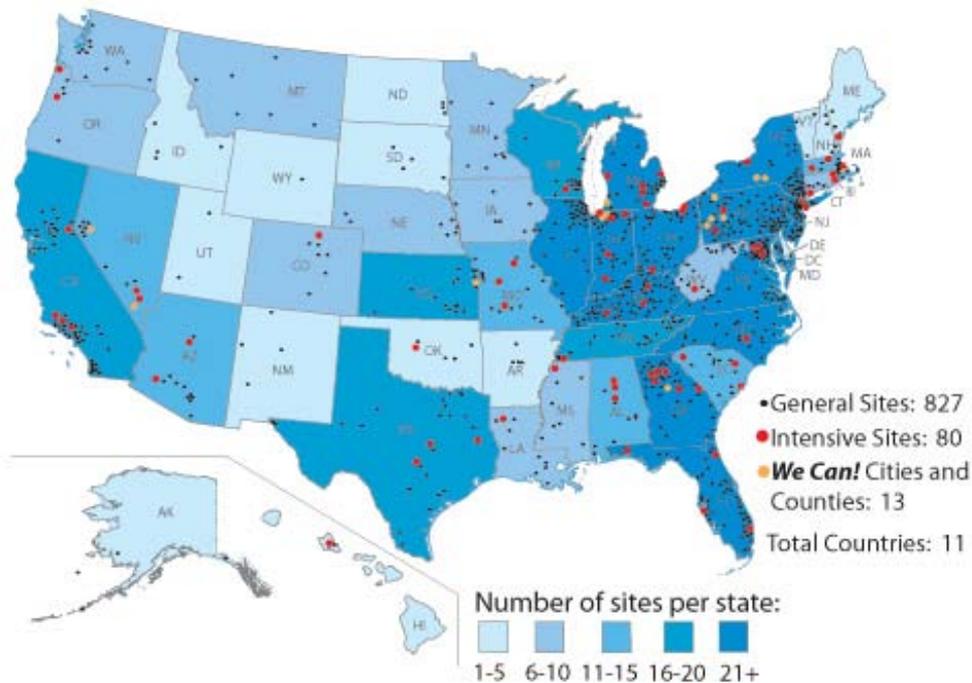
NIH Science working through Communities, Partnerships and Media...

- Communities
 - Curricula
 - Local Partnerships
 - Local Media
 - Outreach Events
- Partnerships
 - Federal
 - Clinical
 - Outreach
 - Media
 - Corporate
- Media
 - Web
 - Print
 - Television

...to help children and families maintain a healthy weight.



We *Can!* Around the Country



- **We Can!** is currently running in 920 Community Sites in 50 states, the District of Columbia, Puerto Rico, the Northern Mariana Islands, and 9 other countries (Australia, Bangladesh, Canada, Fiji, Greece, India, Israel, Nigeria, the Philippines, and Uganda). Settings, include schools, park and recreation departments, hospitals, health systems and public health departments (12 different settings).
- 13 **We Can!** cities, including Boston, Pittsburgh, and Las Vegas are coordinating intensive We Can! programming for employees, parents and youth.
- More than 40 National and Corporate Partners

Summary and Future Research

The NIH Obesity Research Task Force is continuing to pursue trans-NIH research opportunities to advance progress in understanding, preventing, and treating obesity.