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NIH Update: Translating Basic Behavioral Science into New Pediatric Obesity Interventions

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Abstract

Pediatric obesity, which has risen substantially over the past 30 years, increases the risk of later-life obesity as well as the risk of chronic diseases such as cancer, cardiovascular disease and diabetes. Basic research to better understand the biological, behavioral, psychological and social factors associated with excessive weight gain in early life, and studies translating these basic research findings into novel preventive and therapeutic strategies, are essential to our ability to better prevent and treat childhood obesity. This overview describes several NIH efforts designed to stimulate basic and translational research in childhood obesity prevention and treatment and calls for further efforts in these areas. These examples demonstrate the value of research in early-phase translational pediatric obesity research and highlight some promising directions for this important area of research.

Keywords

Basic Behavioral Science; Early-phase Behavioral Translation; Intervention Development; Pediatric Obesity; Obesity-Related Behavioral Intervention Trials (ORBIT) Model

Introduction

Excessive, early weight gain has been found to increase risk for obesity later in life (Freedman et al., 2007; Taveras et al., 2009), and is a risk factor for many diseases, such as cancer, cardiovascular disease, and diabetes (Ogden et al., 2014; Boyer et al., 2015). Pediatric obesity has been rising steadily over the past three decades and, although there is evidence that this increase may be slowing or stabilizing, especially in very young children (Ogden et al., 2014), obesity in childhood remains a significant behavioral risk factor and an important target of NIH funding efforts. In addition, wide disparities in obesity rates remain

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among population subgroups, with minority and low-income children and adolescents showing the highest rates of obesity (Ogden et al, 2014). Thus, an important focus of pediatric obesity research is identifying and implementing more effective interventions to reduce obesity in vulnerable and underserved groups, such as minority and low-income children and families.

NIH support for childhood obesity research spans the translational spectrum, from basic research on the psychological, behavioral, biological and social processes that characterize early childhood development and present potential targets for obesity-related treatments, to studies that translate knowledge about these processes into obesity-related interventions for children, to efficacy and effectiveness trials, and finally, to dissemination and implementation of treatments in clinical and community settings. All of these activities have merit and NIH research in these areas has contributed, along with efforts at local, state and national levels, to recent progress in achieving lower obesity levels in young children (Ogden et al., 2014).

This overview will focus on selected examples of NIH-funded early-phase translational studies that utilize basic behavioral science findings to inform obesity interventions for children at all stages of development, from infancy through adolescence. It is not intended to be comprehensive, as an in-depth review of work in this area is beyond the scope of this article. Instead, by highlighting several promising lines of NIH-supported pediatric obesity research in the basic-to-clinical arena, I hope to illustrate how such research can contribute to efforts to reduce childhood obesity and ultimately, the chronic diseases resulting from it.

NIH Support for Basic and Early-phase Translational Behavioral Research in Pediatric Obesity

Understanding the basic biological, behavioral, social and psychological processes that underlie childhood obesity is key to identification of new treatment targets and the development of more effective interventions to tackle this behaviorally-based risk factor (see Epstein & Wrotniak, 2010 for an excellent overview of basic science findings in pediatric obesity research). Much of the NIH-supported basic behavioral research examining the influence of factors such as cognitive and affective processes, stress and stress reactivity, social relationships and dynamics, and the built environment on obesity-related health behaviors has involved the funding of Investigator-initiated grants and Institute-specific research initiatives (see http://www.obesityresearch.nih.gov/ for information and resources related to NIH's obesity research portfolio, Strategic Plan, and funding opportunities). Recently, however, several large NIH-initiated efforts have been developed that support work in these areas.

NIH Basic Behavioral and Social Science Opportunity Network (OppNet)

In recognition of the importance of basic behavioral research to health, the NIH initiated the *Basic Behavioral and Social Science Opportunity Network (OppNet)* in November 2009 to support research on the underlying basic mechanisms and processes that influence health-related behaviors (http://oppnet.nih.gov/).

Oppnet has supported several lines of research on the psychological, social, cognitive, and neural mechanisms underlying obesity-related behaviors in children. These include investigation of the effects of regular exercise on neural circuitry and brain structure which demonstrated improvements in fronto-temporal white matter integrity (Schaeffer et al, 2014) and alterations in neural circuitry supporting cognitive control (Krafft et al., 2014) in overweight, sedentary children. OppNet-supported research to identify environmental moderators of pediatric weight loss maintenance found that reduced consumption of food eaten away from home was associated with reduced BMI and body fat in children and identified changes in diet quality as a potential mechanism for this effect (Altman et al., 2015). Finally, an OppNet-funded project focusing on links between stress, eating behavior, and obesity in low-income children has sought to identify the biologic and behavioral pathways through which stress may affect obesity in children, for example by potentially increasing sensitivity to food as a reward or reducing ability to delay gratification for food (Lumeng & Miller, PIs, 1R01DK098983). Further details on these and other OppNet-funded projects can be found at http://oppnet.nih.gov/ along with relevant funding opportunity announcements related to basic behavioral science research.

Transdisciplinary Research on Energetics and Cancer (TREC)

The National Cancer Institute's (NCI) TREC program aims to reducing cancer linked with obesity, poor diet, and low levels of physical activity by integrating diverse disciplines to find effective interventions across the lifespan (https://www.trecscience.org/trec/default.aspx). TREC was established in 2005 in response to a growing body of evidence that obesity plays a role in the development of many types of cancer. In the initial phase of TREC (2005 – 2010), four TREC Research Centers and one Coordination Center were funded, each including scientists from multiple disciplines and encompassing projects spanning the basic biology and genetics of behavioral, socio-cultural, and environmental influences on nutrition, physical activity, weight, energy balance, energetics, and cancer risk.

Several TREC projects focused on basic and epidemiological research in children and adolescents that could be used to develop novel obesity-related interventions. For example, a project led by Susan Redline and colleagues at Case Western Reserve University aimed to define the relationship between risk factors such as insufficient sleep and sleep apnea in children and adolescents and changes in both weight and biochemical indices of metabolic pathways implicated in cancer to enable development of targeted interventions for high-risk children. Results from this study demonstrated that chronic insufficient sleep duration, measured longitudinally from infancy to mid-childhood, is associated with lower quality diet in children, with children who had the least favorable diets and sleep duration throughout childhood having the highest estimated BMI *z*-scores, suggesting sleep duration and diet quality as important intervention targets in efforts to prevent childhood obesity (Cespedes et al., 2016).

In another TREC project, researchers at the University of Southern California TREC Research Center, led by Michael Goran and his team, explored the physiological, metabolic, genetic, behavioral, and environmental influences on obesity and cancer risk in minority children. One study in this set of projects, which examined the role of neighborhood-level

factors on progression toward overweight and obesity in children, found a significant relationship over an eight-year period between traffic density and body mass index (BMI) in a cohort of 3318 children living in multiple communities in Southern California (Jerrett et al., 2010). These findings implicate traffic, a pervasive feature of urban environments, as a major but potentially modifiable risk factor for the development of obesity in children, and thus provide important information to guide the development of future environmentally-based pediatric obesity interventions.

Obesity-Related Behavioral Intervention Trials (ORBIT)

Research translating basic behavioral science discoveries such as those mentioned above into new behavioral interventions for behaviorally-based risk factors has not been as well-recognized nor resourced as similar early-phase translational research in the biomedical arena. Especially in the case of obesity, a complex risk factor based on a combination of biological, behavioral, social, psychological and environmental influences, accelerating early-phase translational research is increasingly being viewed as an important area of need.

In response to this need, in 2009 NIH initiated the *Obesity-Related Behavioral Intervention Trials Consortium* (www.nihorbit.org), a trans-NIH cooperative agreement program led by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with the National Cancer Institute (NCI), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the Eunice Shriver Kennedy National Institute on Child and Human Development (NICHD) and the NIH Office of Behavioral and Social Sciences Research (OBSSR). The ORBIT consortium consists of interdisciplinary teams of researchers at seven research sites and a Resource Coordinating Unit (RCU) who are developing and testing novel interventions that translate findings from basic research on human behavior (e.g., habituation, motivation, habit formation, stress, and social networks) into more effective clinical, community, and population interventions to reduce obesity and alter obesity-related health behaviors (e.g., diet, physical activity). Investigators at each site are conducting several types of studies during the 5-year funding period, including formative research, experimental and proof-of-concept studies, and feasibility pilot studies, in order to identify and test promising new approaches to reducing obesity and improving obesity-related behaviors.

The ORBIT program is notable for the diversity of its targeted populations; many of its studies focus on vulnerable and under-served groups, including Latino and African-American adults, African-American adolescents, low-income populations, pregnant women, and women beginning the menopausal transition. The interventions being developed to address obesity and obesity-related behaviors in these groups include a wide range of strategies, including promoting small changes in eating behaviors and physical activity; reducing stress-related eating; improving sleep patterns; increasing motivation to adhere to weight loss strategies; and engaging an individual's social networks and communities to encourage physical activity.

Three of the seven ORBIT sites are focused on children and adolescents: Reynolds and colleagues at Claremont University conducted research to create a novel intervention based on basic behavioral science findings on habit formation and neurocognition to improve

nutrition behavior and reduce risk for obesity in adolescents from low-income families; Naar-King and her team at Wayne State conducted an adaptive 6 month intervention with Community Health Workers using a sequential randomized assignment trial (SMART design) that included skills training modules, motivational conversations and contingency management in African American adolescents and their primary caregivers; and Epstein et al. at the University of Buffalo conducted a series of studies to translate habituation theory into interventions for pediatric obesity by reducing the variety of less healthy, high-energy-density (HED) foods to lower their intake while simultaneously increasing the variety of healthier, low-energy-density (LED) options to increase their intake. Findings and implications from these studies will be discussed below.

The Orbit Model

In addition to the individual ORBIT projects, a major product of the ORBIT consortium has been the development of a framework to guide the behavioral intervention development process. The ORBIT model consists of a phased approach similar to the drug development model but adapted for behavioral treatment development (Czajkowski, Powell, et al., 2015). It encompasses two overarching phases of intervention development, entitled “Phase I” (Intervention Design) and “Phase II” (Preliminary Testing) and each includes two distinct sub-phases. In Phase Ia, treatment targets and components are initially defined, including the degree of change in the treatment target needed to demonstrate a clinically meaningful effect in ultimate health outcome. In Phase Ib, these components are tested and refined to achieve a well-defined treatment “package.” Phase IIa involves “proof-of-concept” testing which aims to determine if the treatment package can achieve a clinically significant degree of change in the pre-specified treatment target; Phase IIb involves further pilot testing using larger samples, randomized designs and a determination of feasibility.

Key features of the ORBIT model include an emphasis on beginning with “with the end in mind” – i.e., starting with a “significant clinical question” from providers, patients or others intimately involved in the behavioral issues and/or disease processes at hand to ensure that the intervention being developed will ultimately have “real world” meaning and impact; using basic behavioral science findings to understand the “drivers” of the behavior or disease being addressed, to identify appropriate and modifiable treatment targets, and define essential interventional components; a focus on achieving not just statistically significant, but clinically meaningful changes in behavioral treatment targets that are tied to prevention or mitigation of disease risk and outcomes; and progression through a series of flexible, increasingly rigorous series of phases using a variety of study designs and methods, as the intervention is designed, refined, optimized and tested, culminating in efficacy and effectiveness trials, and ultimately resulting in dissemination and implementation of an intervention that has a significant impact on clinical endpoints in a clinical and/or community setting.

Science of Behavior Change (SOBC) Common Fund Program

The Science of Behavior Change Program (https://commonfund.nih.gov/behaviorchange/index) is an NIH Common Fund initiative that promotes basic and early-phase translational research on the initiation, personalization and maintenance of behavior change. Several

projects related to pediatric obesity were funded as part of the initial phase of SOBC. An example is work by Lumeng, Miller and colleagues that examines relationships among self-regulation, salivary cortisol and alpha amylase, emotional eating behavior and weight status in low-income toddlers to better understand biobehavioral mechanisms of excessive childhood weight gain, potentially leading to more effective, novel, targeted prevention approaches (https://commonfund.nih.gov/behaviorchange/fundedresearch provides information on this and all SOBC funded research projects).

More recently, SOBC initiated a program of research based on an "experimental medicine approach" to the development of mechanistically-based interventions for preventing and treating unhealthy behaviors linked to disease. This approach is congruent with and expands on the ORBIT model's earliest phase (Phase I) by providing a detailed set of steps for identifying and validating behaviorally-based treatment targets, including: (1) identifying a set of putative targets within a psychological or behavioral domain that is implicated in health behavior; (2) leveraging existing or developing new experimental or intervention approaches to *engage* the targets; (3) identifying or developing appropriate assays (measures) to permit verification of target engagement; and (4) testing the degree to which engaging the targets produces a desired change in health behaviors that lead to clinically significant outcomes or endpoints. One of the projects funded by this program, led by Alison Miller at the University of Michigan, involves measuring childhood self-regulation targets known to be associated with obesity risk and testing whether intervening on these mechanisms can improve self-regulation and adherence to weight management regimens in school-age low-income children (for more information, see https://commonfund.nih.gov/behaviorchange/fundedresearch).

Highlights of NIH-funded Basic and Early-phase Translational Behavioral Research in Childhood Obesity

Infancy & early childhood

Infancy through age five is acknowledged to be a critical developmental period for forming the preferences and habits that contribute to obesity-related dietary and physical activity behaviors. Basic behavioral research has found, for example, that at an early age, children heavier for their height prefer food to alternative reinforcers (Kong et al., 2015) and that obese infants find food more reinforcing than their leaner peers (Temple et al., 2008).

A better understanding of the underlying biological, behavioral, social and psychological factors that predict excessive weight gain in very young children is increasingly being seen as an important part of NIH efforts to reduce childhood (and later life) obesity. In November of 2013, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) held a Workshop on "*The Prevention of Obesity in Infancy and Early Childhood*" to identify what is known about preventing obesity in early childhood and what needs to be done to accelerate research targetting this important developmental period. Citing significant gaps in knowledge concerning the basic biological and behavioral factors underlying excessive weight gain in the birth through 2 year age period, Workshop participants recommended that research in this area be accelerated (b et al., 2015), resulting in release of an NIDDK-led,

trans-NIH program announcement (PAR-14-323) "*Understanding Factors in Infancy and Early Childhood (Birth to 24 months) that Influence Obesity Development*" (http://grants.nih.gov/grants/guide/pa-files/PAR-14-323.html).

The value of basic and early-phase translational research in very young children was illustrated in a recent Expert Panel meeting convened by the Office of Behavioral and Social Sciences Research (OBSSR) on "*Self-regulation of Appetite*," held in July, 2015 on the NIH campus in Bethesda, Maryland. The meeting included presentations by several researchers who have published extensively on the biological, social and psychological bases for eating behaviors in infancy and early childhood.

An example of research in this area is that conducted by Mennella and colleagues who have explored the nature and consequences of very early taste preferences – e.g., preference for sweet and aversion to bitter tastes – which in an environment rich in added sugars and salt, can lead to overweight and obesity (Mennella & Bobowski, 2015; Mennella et al., 2014; Drewnowski et al., 2012).

In a similar vein, Birch and colleagues have examined the importance of early learning in shaping infant and young children's taste preferences, showing that with repeated exposure even initially rejected new foods can become accepted and liked (Savage et al., 2013; Sullivan & Birch, 1994; Birch & Marlin, 1982). These researchers have also demonstrated the influence of factors such as temperament, self-regulation capacity, and parental feeding on infants' food intake and risk for obesity (Anzman-Frasca et al., 2013; Anzman-Frasca et al., 2012; Birch et al., 2003), and have translated this research into a set of responsive parenting practices related to feeding – e.g., provision of alternatives to food as "soothing" behaviors for infant fussiness, increased sleep duration, awareness of hunger/fullness cues, use of repeated food exposures, delay in introducing solid foods. In a pilot study, infants randomized to these responsive parenting interventions were found to have lower weight-for-length at 1 year (Paul et al., 2011), demonstrating the promise of this approach for reducing obesity risk in infants.

Later Childhood and Adolescence

NIH support for studies that elucidate the psychological, social, cognitive underpinnings of obesity-related behaviors in children and their families, along with support for the design and testing of interventions based on these findings, has resulted in the development of several evidence-based, efficacious treatments for pediatric obesity (Coppock et al., 2014; Wilfley et al., 2007a). A particularly fruitful program of research by Epstein et al. and colleagues incorporates both children and their parents in a family-based treatment (FBT) that has been shown to be highly efficacious (.e.g., Epstein et al., 1990; Epstein et al., 2007). The approach uses concepts from basic behavioral research, such as contingency contracting, self-monitoring of weight and food intake, mastery of behavior change, behavioral choice theory, and stimulus control management, among others (Epstein et al., 1998).

Building on the FBT model to address maintenance of weight loss in children, Wilfley and colleagues have developed a social facilitation maintenance treatment (SFM) that promotes

healthy eating and physical activity following the end of active FBT through extended parent and peer support, improvements in body image, and help in responding to teasing, and that has been shown to achieve maintenance of some degree of weight loss (Wilfley et al, 2007b). Based on further basic behavioral research showing that previous learned behaviors are highly resistant to extinction and continue to exist alongside newly learned behaviors (Bouton, 2002; Bouton et al, 2006), these investigators have enhanced SFM (SFM+) to incorporate the practicing of newly learned behaviors in multiple contexts to ensure long-term establishment of new, healthier eating and activity habits (Wilfley et al., 2010).

Findings from the ORBIT consortium show how translating concepts from basic behavioral research can result in the development of new, innovative approaches to childhood obesity as well as the addition of new components to existing approaches, thereby bolstering their efficacy. For example, Reynolds and colleagues are developing a new intervention based on basic behavioral research on the formation and maintenance of eating habits in low-income adolescents. The investigators used ecological momentary assessment (EMA) to identify physical, social and intrapersonal cues associated with consumption of sweetened beverages and sweet and salty snacks among adolescents. Results showed a number of linkages of cues with snack choices, including that being at school, with friends and feeling lonely or bored were associated with having unhealthy snacks and drinks, while sweetened drink consumption was associated with engaging in physical exercise (Grenard et al., 2013). These findings provide insights into the eating and activity behaviors of high-risk adolescents that can be incorporated into the development of interventions to disrupt these cue-behavior linkages, which is the goal of this line of research.

An example of using basic behavioral science findings to develop novel approaches that can increase the potency of existing interventions is demonstrated by Epstein et al. at the University of Buffalo ORBIT site. This research team utilized the psychological construct of habituation, based in learning theory, to test the effects of varying foods at the dinner meal to reduce energy intake. Basic research has shown that increasing variety increases energy intake, and repeated consumption of the same food increases habituation to those foods and reduces consumption. In one of the trials conducted by Epstein et al. (2015), 24 families with overweight/obese 8–12 year-old children and overweight/obese parents were randomly assigned to 6 months of usual family based treatment (FBT) or FBT plus reduced variety of high energy-dense foods (FBT+Variety). Results showed significant differences between the two conditions in child percent overweight and parent BMI, with positive relationships between child zBMI and parent BMI changes and between reductions in food variety of high energy-dense foods and reductions in child zBMI and parent BMI. These pilot data suggest that reducing the variety of high energy dense foods and repeating meals within the context of FBT, both of which are relatively easily implemented within family-based weight loss treatment, may enhance weight loss in children and their parents, but further work is needed to replicate this finding in larger samples and over longer periods of time.

In another ORBIT project, investigators at the Wayne State site conducted an adaptive behavioral treatment for African American adolescents with obesity (Naar-King et al, 2015) in which 181 youth ages 12–16 years with primary obesity and their caregiver were first randomized to 3 months of home-based versus office-based delivery of motivational

interviewing plus skills building and after 3 months, nonresponders to first phase treatment were rerandomized to continued home-based skills or contingency management. There were no significant differences in primary outcome between home-based or office-based delivery or between continued home-based skills or contingency management for nonresponders to first-phase treatment, though families receiving home-based treatment initially attended significantly more sessions in both phases of the trial, and families receiving contingency management attended more sessions in the second phase. Overall, participants demonstrated decreases in percent overweight over the course of the trial (3%), and adolescent executive functioning moderated this effect such that those with higher functioning lost more weight. Results also showed that older children in the home-based contingency monitoring condition showed the greatest decreases in percent overweight, while younger adolescents responded more strongly to the home-based skills-development sequence (Naar-King et al., 2015). These results suggest it may be important to target psychological factors in obesity treatment, such as executive function; that age is a key variable in tailoring treatments; and that at-home treatment with contingency management may increase session attendance for this vulnerable population.

Research on the relationship of executive functions and eating behavior in childhood and adolescence is a particularly promising avenue of investigation, since a growing body of research has found that the ability to regulate emotions, delay gratification, develop future plans, and avoid or mitigate impulsive actions are critical elements in establishing healthy diets and promoting healthy weight gain from childhood through adolescence and into adulthood. This is exemplified by long-term follow-up studies of Mischel's research on delay of gratification in 4-year olds in which longer delay of gratification at age four has been shown to be related to a lower body mass index (BMI) 30 years later (Schlam et al., 2012). Several lines of research have investigated the mechanisms through which deficits in executive and neurocognitive function are linked to obesity-related behaviors such as dietary intake in children and adolescence (Miller, Lee & Lumeng, 2015; Liang, Matheson, Kaye & Boutelle, 2014; Reinert, Po'e & Barkin, 2013), setting the stage for the development of behavioral interventions designed to improve children's self-regulatory skills (Miller et al., 2012).

A related line of research focuses on the relationship of factors such as food reinforcement, delay discounting and impulsivity to food intake and obesity risk in children (Best et al., 2012; Francis & Susman, 2009; Seeyave et al., 2009). Research showing the importance of delay discounting (a measure of impulsivity, i.e., the tendency to over-value present over future rewards) to food intake has led to development of interventions that encourage more forward-looking or prospective thinking in individuals prone to impulsivity as a way to promote better decision-making. One such strategy, episodic future thinking (EFT), has been shown to reduce delay discounting and energy intake in adults (Daniel et al., 2013) as well as in overweight/obese children (Daniel et al., 2015), thus suggesting a new avenue for improving obesity treatment outcomes in children.

Summary/Discussion

Research translating the biological, behavioral, social and psychological “drivers” of childhood obesity into novel preventive and therapeutic interventions in children is essential to the development of more effective pediatric obesity interventions. In recognition of this need, the NIH supports Investigator-initiated and Institute-initiated basic and early-phase translational research on pediatric obesity using a variety of funding mechanisms, including Investigator-initiated grants and trans-NIH and Instituteinitiated research programs.

Funding for basic and translational research has been shown to be critically important in developing successful child and family treatments for obesity, and is necessary for future progress in this area. In addition to overall support for basic-to-clinical translational research, special attention should be paid to designing and testing novel interventions to address the behavioral, social, psychological and environmental factors that create higher obesity risks and poorer outcomes in minorities and low-income children. Although some of the programs discussed above have included studies that target these groups, given the continuing high rates of obesity and related diseases in ethnic/racial minorities and low-income children and families, future research should especially focus on developing more effective obesity preventive and therapeutic interventions for these vulnerable subgroups.

Given recent advances in basic behavioral and social sciences research, we are poised for a new era in which new knowledge gained from the basic biological and behavioral sciences can be used to continually “refresh” the pipeline so that more powerful preventive and therapeutic treatments for childhood obesity can be developed, ultimately reducing obesity rates in both children and adults and lowering obesity-related risk for chronic diseases later in life.

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Key Points

- Pediatric obesity is a common and important risk factor for future obesity and for chronic diseases.
- Basic research to understand the fundamental “drivers” of childhood obesity and early-phase trials that translate this knowledge into novel interventions to prevent or reduce obesity are important for accelerating the development of new, more effective obesity-related treatments for children.
- The NIH supports both basic and early-phase translational behavioral research related to pediatric obesity through a variety of mechanisms, both solicited and unsolicited.
- Findings from NIH-supported research in basic and early-phase translational behavioral science are producing new discoveries – for example, in areas such as early taste preferences, self-regulation, impulsivity and the reinforcing value of food – that can be used to develop novel targets for pediatric obesity interventions.
- NIH programs, such as ORBIT, and frameworks, such as the ORBIT model, are useful for facilitating the translation of basic behavioral findings into pediatric obesity-related interventions.
- Continued NIH support for basic and translational behavioral science is critical to further progress in developing, testing and ultimately implementing new and more effective interventions to reduce pediatric obesity.