

## Pediatric obesity prevention: From naïve examination of energy imbalance towards strategies that influence the competition for nutrient resources among tissues

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### Abstract

Current pediatric obesity interventions have collectively yielded relatively unsuccessful results. In this Field of Vision, we present plausible physiologic underpinnings fostering ineffectiveness of conventional strategies grounded in requisite induction of negative energy imbalance. Moreover, such recommendations exacerbate the underlying metabolic dysfunction by further limiting metabolic fuel availability, lowering energy expenditure, and increasing hunger (recapitulating the starvation response amid apparent nutritional adequacy) which precede and promote obesity during growth and development. The qualitative aspects of musculoskeletal system (*i.e.*, endocrine response, muscle functional capacity) are likely to improve metabolic function and increase nutrient delivery and utilization. An intricate and complex system including multiple feedback mechanisms operates to homeostatically regulate energy balance and support optimal body composition trajectories and metabolic health, during growth and development. Thus, ignoring the interdependencies of regulatory growth processes initiates a nuanced understanding of energy regulation and thus misguided attempts at preventive strategies. Importantly, these gains are not dependent upon weight-loss, rather we suggest can be achieved through resistance training. Collectively, optimizing musculoskeletal health *via* resistance training elicits augmentation of competitive capacity across systems. Further, substantial gains can be achieved in skeletal muscle mass, strength, and functional capacity through resistance training in a relatively short period of time.

**Key words:** Childhood obesity; Metabolic control; Energy balance; Resistance training; Effective intervention strategies; Weight loss; Musculoskeletal health

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**Core tip:** As obesity-related recommendations stand today, most are unproven and ineffective. While energy balance is an integral component, the etiology of pediatric obesity is a consequence of adipocytes "out competing" other cell types (*e.g.*, myocytes, osteocytes, hepatocytes) for energy. The cumulative effect of fat storage, energetically less costly is at the expense of optimal development of other tissues. The out-competition, due to hyperplasia and hypertrophy of adipocytes impairs physiologic pathways producing metabolically compromised obese children irreversible with "simple" energy balance paradigms. *Via* the activation of endocrine and paracrine effects of the musculoskeletal system, resistance training may be an effective strategy to improve health independent of initial weight loss. However, forced stress on the system is requisite (*e.g.*, resistance training). Resistance training induces systemic anabolism and enhances nutrient delivery and utilization, which are integral in optimizing metabolic control and body composition during growth and development, and in turn overall lifelong health.

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## INTRODUCTION

The presage of pediatric obesity inducing a decline in life expectancy<sup>[1,2]</sup> has evoked calls for expert committees to direct stakeholders on how to best proceed with comprehensive prevention/intervention platforms. However, despite persistent calls for evidenced based policies, current dietary and physical activity interventions have collectively yielded a fairly unsuccessful paradigm. Herein, we provide a potential explanation for the chasm between the resource allocation to "combat" the pediatric obesity epidemic and improvement in health outcomes. As an exhaustive analysis of all pediatric obesity strategies, to date would be infeasible. Thus, the purpose of this Field of Vision is to highlight the conventional strategies and adoption of recommendations written by "expert committees" for governments or health authorities of the United States<sup>[3]</sup>, United Kingdom<sup>[4]</sup> and Canada<sup>[5]</sup>, the Institute of Medicine<sup>[6]</sup> and World Health Organization (WHO)<sup>[7]</sup> as well as Cochrane reviews<sup>[8,9]</sup> (largely grounded in inducing negative energy imbalance through increasing

physical activity and dietary restriction) as naïve approaches to pediatric obesity prevention.

## NAIVE EXAMINATION OF ENERGY IMBALANCE?

Despite endorsements of dietary and physical activity recommendations, the vast majority of interventions to date have had null findings. For example, in 2005, the American Medical Association, the Health Resources and Service Administration, and the Centers for Disease Control and Prevention (CDC) asked representatives from 15 national healthcare organizations to form an expert committee to make recommendations regarding the treatment of childhood and adolescent obesity. The expert committee determined the main foci should include: setting daily eating and activity goals for their overweight or obese children (increased expenditure), increasing consumption of fruits and vegetables (F and V) (modifying intake); minimizing sugary drinks (reduce calories); limiting screen time to  $\leq 2$  h (modifying sedentariness); attaining  $\geq 1$  h. physical activity (increased expenditure); encouraging primary care providers to more closely monitor these target behaviors and goals, and facilitating more explicit planning by parents to achieve weight loss. Similarly, Obesity Canada, convened a panel of experts to create clinical practice guidelines for Canadian health policy. The Steering Committee and Expert Panels in the United Kingdom and Canada reviewed the literature and several years later published their guidelines, which were very similar to those of the United States<sup>[10,11]</sup>. Since 2007, all governments in the United Kingdom have had action plans to reduce pediatric obesity prevalence<sup>[12]</sup>. The WHO globally led the charge indicating that reducing the consumption of high-calorie, energy-dense foods, including sugar-sweetened beverages, increasing the consumption of F and V; and increasing the initiation, duration, and exclusivity of breastfeeding represent comprehensive strategies for reducing pediatric obesity<sup>[7]</sup>. While we do not argue that these approaches have a reasonable basis with theoretical rationale, empirical evidence supporting implementation of any of the aforementioned for improved health outcomes have not been documented and in some instances proven to be ineffective<sup>[13]</sup>. Indeed, investigations linking pediatric obesity and early onset metabolic disease has substantiated developmental origins of disease. Despite a vast body of recommendations generated through these working groups, antiquated application of science has led to the promotion of non-evidence based, and sometimes anecdotal application of simple solutions to a complex problem. Furthermore, such unproven, unfiltered and inconsistent messages guiding pediatric weight management strategies persist despite absence of scientific supporting evidence and ultimately have contributed to a culture of confusion and disinterest. We clearly need a much more balanced approach to

discussing energy flux and long-term health. Conversely, very little attention has been devoted to determining those physiological factors characteristic of early life that could be protective to health and contribute to mitigating age-associated morbidities. While physical inactivity and the consequent adverse effects on fat storage and energy metabolism across the life course<sup>[14-19]</sup>, may be more pathologic during development, this critical period also represents a stage in which capitalization on the benefits of body composition may be attained.

## FAILURE OF WEIGHT LOSS STRATEGIES

We conjecture that the failure of weight loss strategies to improve health in the pediatric population is grounded in the fundamental assumption that inducing negative imbalances *via* caloric restriction and energy expenditure circumvent excessive fat storage during growth and development. Indeed, energy balance plays a role; however, during growth and development excess fat storage is a consequence of adipocytes "out competing" other cell types (e.g., myocytes, osteocytes, hepatocytes) for energy due to lack of engagement of other cell types in the competition for energy<sup>[16-18]</sup>. Over the three decades encompassing the pediatric obesity "epidemic", sedentary behaviors have increased drastically, with the vast majority of free time spent by children in light activity or relatively inactive and engaged in limited (if any) moderate to high-intensity activities. During the anabolic growth stage, failure to engage skeletal muscle, as a primary tissue in the regulation of fuel utilization and delivery, in greater than day to day threshold promotes metabolic compromise. In turn, the endocrine and paracrine effects of the musculoskeletal system in which contraction greater than the "typical day to day threshold" is requisite are attenuated, while the endocrine effects of adipose tissue are up-regulated. Dietary restriction, in the absence of muscle contract, further increased sensitivity of adipokines to promote fat storage<sup>[18,19]</sup>. This conceptualization is strongly supported by extant research, given those increments in fat mass are a function of adiposity, adipocyte number is a primary determinant of obesity, and early pubertal development is a major determinant of adipocyte number and lifelong obesity risk<sup>[19]</sup>. Thus, modifying diet and/or engaging in low-intensity physical activity programs in which mechanical stress is not requisite, does not generate competitive inclusion of osteo-/myo-cytes. As such, the competitive advantage of adipocytes and ensuing loss of metabolic control due to lack of participation by the musculoskeletal system is nearly impossible to counter. The cumulative effect of nutrient partitioning to adipose at the expense of other tissues in concert with a greater number of adipocytes and impaired glucose and lipid metabolism produce metabolically compromised children predisposed to inactivity, metabolic dysfunction and obesity irrespective of short-term weight loss strategies. In this context, it is naïve

to suggest that limiting availability of nutrients without enhancing utilization capacity. According many of the recommendations to date represents a futile process enhancing adipocyte dominance rather than attenuating it, with particular salience during the dynamic metabolic sequelae of critical periods in development (e.g., the pubertal transition).

## ABSENCE OF MUSCLE CONTRACTION

Notably, increasing daily activity by children does not merely characterize play, but encompasses an essential component of healthy growth and development. Optimal musculoskeletal development is derived from complex integration of cellular and systemic autocrine, paracrine and endocrine factors that promote the capacity to sustain work. Thus, enhanced musculoskeletal function *via* augmenting metabolic crosstalk has the capacity to improve whole body metabolism including insulin-stimulated glucose uptake, lipolysis, and resting energy expenditure in addition to improving musculoskeletal function and overall health. Substantial evidence in animals and humans highlight the great detriment of physical inactivity. For example, after 4-h of inactivity (tail suspension), a functional decline in lipoprotein lipase (LPL) activity accompanied by decreased skeletal muscle triglyceride clearance, lower HDL and attenuated muscle oxidative capacity with immediate decline in musculoskeletal function has been observed<sup>[16-18]</sup>. Occupational studies indicate workers who sat most of the day have about twice the rate of cardiovascular disease as those demanding more standing and ambulatory activities<sup>[18]</sup>. Moreover, human bed rest investigations revealed that one-to-three weeks of bed rest in otherwise healthy, active men had a more profound impact on physical work capacity than did three decades of aging in the same men<sup>[15,16]</sup>. Within days, decreased muscle activity due to prolonged bed rest decreased skeletal muscle insulin sensitivity, insulin signaling, fitness, leg muscle mass and increased intra-abdominal fat<sup>[16]</sup> and reduced insulin signaling, altered glucose and lipid metabolism and increased central adiposity even in the absence of weight-loss. We acknowledge that bed rest is an extreme model of inactivity and does not accurately mimic the low levels of physical activity that even most sedentary individuals undergo on a daily basis. However, the minimal 8 h a day of sitting in today's youth in school (not to mention the well-documented low levels of activity in the home environment) may in legitimately represent a degree of such extreme inactivity.

Importantly, the capacity for skeletal muscle to fulfill its essential role in governing glucose and lipid oxidation is largely attributable to stimulation of contractile forces which exceed the day-to-day threshold of skeletal use. Stimulation by contractile forces enhances the synthesis and release of skeletal muscle peptides which participate in a variety of metabolic actions<sup>[14,17]</sup>. A shift in paradigm is desperately needed.

## SHIFT IN PARADIGM

Enhancing nutrient utilization rather than diminishing nutrient availability (e.g., negative energy balance) can be more readily accepted with improved adherence. Thus, germane to our proposed shift in paradigm, contraction-dependent endocrine effects of skeletal muscle have been shown to improve metabolic parameters and offer a means of improving nutrient delivery and utilization. Importantly, these gains are not dependent upon weight-loss, rather we suggest can be achieved through resistance training. Relative to the commonly prescribed aerobic exercise, resistance exercise: (1) evokes a lower perceived exertion and is more readily accepted among obese individuals; (2) requires less cardiorespiratory capacity in the initial phases (rather short bouts of effort); and (3) activates anabolic processes leading to musculoskeletal hypertrophy. Collectively, optimizing musculoskeletal health elicits augmentation of competitive capacity of myocytes, osteocytes and hepatocytes. Further, substantial gains can be achieved in skeletal muscle mass, strength, and functional capacity through resistance training in a relatively short period of time. While the sense of urgency is now at the pinnacle, evidence of the emergence of the dire health effects caused by inactivity has been steadily mounting for several decades<sup>[2,20]</sup>. The reduced activity in contemporary youth apparent from the early 1970s to present has substantially altered growth-related outcomes in the pediatric population<sup>[21-26]</sup>. This is as evidenced by progressive and cumulative increases in height<sup>[22,23]</sup>, body mass<sup>[24]</sup>, bone mass, organ mass, and fat mass/adiposity<sup>[25]</sup> as well as earlier onset and progression of chronic diseases. As these metabolically compromised children mature and transition through puberty and the adverse effects of physical inactivity manifest<sup>[27]</sup>, the competitive advantage of adipocytes increases, underlying the poor health and well-being prognostication of future generations. To move forward, future research and subsequent recommendations may be most productive if directed away from naïve examination of energy balance and redirected towards intervention/prevention strategies that influence the competition for nutrient resources among tissues.

## CONCLUSION

The reliance on conventional strategies for decreasing pediatric obesity prevalence continues despite decades of unequivocal evidence. While, in theory, inducing negative energy imbalance seems logical, targeted efforts have been largely ineffective in sustained weight management and/or improvement in health outcomes. Herein, we explored the chasm between the current recommendations in the pediatric population driving approaches, exposing where lack of science-based direction has led to futility and propose a potential paradigmatic shift away from the adipocentric focus encompassing developmental origins of disease

towards capitalizing on the substantive aspects of health during childhood. Cumulatively, work to date has vastly improved our knowledge of the complex nature of pediatric obesity and led to the identification of mechanisms underlying a competitive advantage of adipocytes during growth, however, an effective strategy to promote health outcomes in the contemporary obesogenic environment remains elusive. We contend, the failure of weight (fat) loss strategies in the pediatric population is grounded in a requisite negative energy imbalance for improving health outcomes. While weight management is imperative, we posit that induction of negative energy imbalance should not be the main, and certainly not the only, focus for treatment of the obese child for promotion of metabolic improvement. As such, the persistent dependence on caloric restriction and the prescribed about 60 min per day of aerobic activity has demonstrated that adherence, and consequent long-term weight management and metabolic health improvements are minimal. Thus, to move forward, future research and subsequent recommendations may be most productive if directed away from naïve examination of energy balance and redirected towards intervention/prevention strategies that enhance nutrient partitioning to tissues (*i.e.*, myocytes, hepatocytes, osteocytes, *etc.*). It is well-established that chronic inactivity pathologically elicits adipocyte storage feedback mechanisms (e.g., hyperplastic adiposity, intensified pancreatic  $\beta$ -cell function, impaired skeletal muscle function), increasing the risk of metabolic disease, cardiovascular incidents and some cancers. However, inducing resistance to the musculoskeletal system exerts contractile forces which enhance the synthesis and release of peptides released from muscle, bone and liver which participate in a variety of beneficial metabolic actions, including enhancing glucose uptake and lipid oxidation. Further, nutrient utilization and delivery and in turn, metabolic profile can be improved *via* improving the signaling from other tissues. Importantly, these feed forward metabolic actions can be achieved even in the absence of weight-loss, and without negative energy imbalance.

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