



Published in final edited form as:

Mayo Clin Proc. 2013 June ; 88(6): 593–604. doi:10.1016/j.mayocp.2013.04.005.

Scientific Decision Making, Policy Decisions, and the Obesity Pandemic

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Abstract

Rising and epidemic rates of obesity in many parts of the world are leading to increased suffering and economic stress from diverting health care resources to treating a variety of serious, but preventable, chronic diseases etiologically linked to obesity, particularly type 2 diabetes mellitus and cardiovascular diseases. Despite decades of research into the causes of the obesity pandemic, we seem to be no nearer to a solution now than when the rise in body weights was first chronicled decades ago. The case is made that impediments to a clear understanding of the nature of the problem occur at many levels. These obstacles begin with defining obesity and include lax application of scientific standards of review, tenuous assumption making, flawed measurement and other methods, constrained discourse limiting examination of alternative explanations of cause, and policies that determine funding priorities. These issues constrain creativity and stifle expansive thinking that could otherwise advance the field in preventing and treating obesity and its complications. Suggestions are made to create a climate of open exchange of ideas and redirection of policies that can remove the barriers that prevent us from making material progress in solving a pressing major public health problem of the early 21st century.

Obesity represents a complex set of medical, public health, social, and economic problems that have been refractory to study and effective problem solving. Herein we outline a variety of issues that lie at the heart of our inability to understand the fundamental nature of the problem and that impede inquiry aimed at developing effective solutions.

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Potential Competing Interests: Dr Allison has received grants, donations to his university, and consulting payments from numerous nonprofit and for-profit organizations with interests in obesity, including the National Institutes of Health, National Science Foundation, Federal Trade Commission, Food and Drug Administration, private foundations, pharmaceutical companies, food companies, beverage companies, litigators, and publishers. Dr Blair has received grants and consulting payments from organizations such as the National Institutes of Health, food companies, beverage companies, publishers, and equipment companies.

ISSUES AND CONCERNS

Obesity Is a Pandemic

Many developed countries and more affluent sectors of emerging economic powers are experiencing a marked increase in the prevalence of overweight and obesity.^{1,2} The implications of this epidemic for human health, productivity, and health care costs are ominous.^{3,4}

In response to the unfolding crisis, funding of obesity research has increased. For example, the US National Institutes of Health annual funding of obesity research is now nearly \$1 billion,⁵ and the combination of nutrition and obesity research has grown to more than \$2 billion per year. Despite this outpouring of resources, the listing of 233 categories of research funding does not include a category for physical activity (PA) or exercise.⁶ Although this research investment has led to some advances in understanding the genetic, physiologic, and behavioral correlates of obesity, our ability to treat obesity has increased only modestly outside of surgical interventions and potentially a few newly approved pharmacologic agents, and our ability to prevent obesity at the population level has yet to be demonstrated.⁷ Prevalence in the general population remains very high, and the recent flattening of rates in the United States is not, by generally accepted scientific standards, attributable to any public health initiatives.⁸⁻¹⁴

We propose that greater success in this domain may be achieved by overcoming 3 overarching and, to some extent, intersecting shortcomings, each with policy implications: (1) a lack of conceptual clarity in defining obesity, (2) a range of methodologic issues that encourage generating data that perpetuate misconceptions about obesity's causes, and (3) scholarly dialogues, including peer review processes, that uncritically accept a priori assumptions about cause derived from inaccurate models of obesity and inadequate evidential foundations (Tables 1 and 2). Each of these overarching flaws is associated with a set of policy directives and *ad hoc* decisions that have contributed to dampening interest in plausible alternatives to conventional explanations as to the causes of and solutions to the obesity epidemic.

Major Presumptions and Myths About Obesity

Recently, several articles¹⁹⁻²³ have pointed out that there are many unproven beliefs (presumptions) and disproven beliefs (myths) about obesity erroneously circulating as facts not only in the mass media and the general public but also in the scientific community. Furthermore, these articles suggest some of the factors that may lead to the propagation of these erroneous beliefs. Table 2 provides a nonexhaustive list of examples, quoted or adapted largely from the article by Casazza et al.¹⁹

Defining Obesity: Need for Conceptual Clarity

Obesity is defined differently in various disciplines and, with these variations in definition, individuals, therefore, will be classified differentially. For example, physiologists and researchers working with animal models will classify a subject as obese in terms of absolute or relative (percentage) body fat (BF). Indeed, among individuals in this group, the terms *obesity* and *adiposity* are used interchangeably. However, following the lead of public health practitioners, clinicians, some clinical researchers, and epidemiologists, obesity is typically categorized on the basis of a body mass index (BMI [calculated as the weight in kilograms divided by the height in meters squared]) of at least 30.²⁴ Indeed, when obesity statistics are cited, invariably they are based on the convention of defining individuals with a BMI of at least 30 as obese. On the basis of relatively easily obtained measurements of height and weight, BMI has been used for many decades by clinicians, epidemiologists, and actuaries

as a simple estimate of relative weight that can predict health-related outcomes.^{25–29} Although it is assumed that the single universal attribute of obesity, defined as a BMI of 30 or greater, is an excess accumulation of adipose tissue, it is clear that BMI is composed of much more than fat mass.³⁰ Over the decades, this has led to debate on the utility of relying on BMI to describe obesity^{31–33} and to enhancements to increase its utility.^{34–36}

Notwithstanding the problems inherent in equating a BMI of 30 or greater with obesity, and then making an implicit assumption that those categorized as obese have excess adipose tissue, this extreme state of overweight is a heterogeneous array of physiologic and behavioral adaptations to environmental conditions.³⁷ Not all people with high levels of BF are obese by this classification; likewise, some people with very high BMIs may have little fat mass. For example, females tend to have much higher levels of BF than their male counterparts at all levels of BMI³⁸; yet, their obesity rates, as defined by a BMI of at least 30, are not generally much higher than those of males.³⁹ In contrast, some individuals (eg, certain categories of elite athletes) may have little BF but BMIs that define them as obese.⁴⁰

Even in most instances in which adiposity is its main driver, obesity is not a single pathologic condition but rather a sign of underlying primary pathologic abnormalities.^{41,42} Clearly, obesity arises from the dynamic interplay of the external environment,^{43–45} inclusive of the social milieu, built environment, and food energy availability^{46–48}; behavioral and developmental processes^{49,50}; and a variety of genes and epigenetic effects that, in turn, control a myriad of metabolic systems and subsystems that regulate body composition, energy intake (EI) and energy expenditure (EE), and nutrient partitioning.^{51–53} Although intrinsic (eg, individual genetic and metabolic) factors may play a role in determining who may become obese,^{54,55} the preponderance of epidemiologic and ecological evidence indicates that social and environmental factors that determine energy balance (EB) are the primary causes of the secular shift toward higher body weights.^{56,57}

Definitional issues notwithstanding, characterizing obesity as a distinct condition suggesting a simple, straightforward, and unvarying etiology has biased all phases of obesity-related discourse. Consequently, it has generated a futile search for a single explanation, thus promoting excessively optimistic and generally ineffective interventions and other misguided attempts in the vain hope for “magic (eg, pharmacologic) bullets.” Although BMI provides a reasonable, if crude, estimate of adiposity at the population level, it has little value as a dependent measure in studies of obesity prevention and treatment because changes in body weight may be indicative of alterations in muscle mass, organ mass, other lean body mass, fat mass, body water, glycogen stores, or combinations of these. Therefore, studies reporting decreases in body weight also may exhibit increments in adiposity (ie, percentage fat mass) and decrements in lean body mass.^{58,59}

Nevertheless, a recent meta-analysis using BMI to determine overweight and obesity status was performed with data from 97 major epidemiologic studies in nearly 2.9 million people with 270,000 deaths during follow-up.⁶⁰ Although this study found that the entire population of obese individuals had a significantly higher mortality rate than did those with a normal BMI (Hazard ratio [HR] = 1.18 [95% CI, 1.12–1.25] for obesity [all grades combined]), this was not the case with class I obesity (BMI, 30.00–34.99), which did not have higher mortality rates and actually had 5% lower mortality than did the normal BMI group (18.50–24.99), which was not quite significant statistically. However, the lowest mortality rate occurred in the overweight BMI group (25.00–29.99), with 6% lower mortality compared with the normal BMI group. Obese individuals 65 years and older had no higher mortality rates compared with normal-weight persons, and this applied even to those with a BMI of 35.00 or greater. These findings from a large metaanalysis of cohort data call into question what is an optimal BMI in current populations.

Obesity Paradox

To add to the existing confusion and controversy, the obesity paradox has been well described during the past decade.⁶¹ Overweight and obesity, generally described by BMI criteria, are associated with an increased prevalence of almost all cardiovascular disease (CVD) risk factors and of almost all CVDs, including hypertension, coronary heart disease (CHD), heart failure, and atrial fibrillation. Despite this association, considerable evidence now indicates that overweight and obese patients with the same CVD diagnoses have better short- and long-term prognoses than do their leaner counterparts. Although it was theorized that this paradoxical relationship may be explained, in part, by the relatively weak relationship between BMI and BF, recent studies have found the obesity paradox with BMI, BF, and even measures of central obesity.^{61–64}

Adding to the literature reporting the obesity paradox with BMI, we recently found that the highest mortality rates, at least in patients with CHD, are concentrated in those with the lowest levels of lean body mass, suggesting that this may be as much a lean paradox as it is an obesity paradox.^{62,64} Nevertheless, in patients with CHD⁶³ and in those with heart failure,⁶⁵ it seems that physical fitness significantly alters the relationship between adiposity and subsequent prognosis such that only those with low levels of fitness demonstrate this obesity paradox. Patients with high fitness, regardless of their level of adiposity by BMI, BF, and central obesity, have a favorable prognosis.^{61,63,65} Although further research is needed to determine optimal levels of body composition in patients with CVD, the present data indicate that the greatest attention needs to be directed toward increasing fitness, which is generally obtained with increases in PA and EE, rather than reducing adiposity *per se*. With respect to CVD, the obesity paradox reflects the complexity of these relationships.

Scientific Standards, Assumptions, Methods, and Discourse Limiting

Examination of Alternative Explanations of Cause Presumption—Most scientific theories and models of obesity are based on the first law of thermodynamics (FLT) and proffer that imbalances between EI and EE lead to changes in energy storage (primarily as lipid). The imprecision of current methods for measuring EI^{66–70} and EE^{71–73} on a large (ie, public health) scale precludes accurate quantification of the EB equation and thus preclude definitive statements regarding the cause of the obesity epidemic.

Description vs Explanation—The FLT provides a true but inadequately simplistic and inherently tautological description of the energy imbalance that leads to overweight and obesity. The “criteria for judging causality,” developed by Hill^{74,75} in the early 1950s to provide a framework for assessing cause in complex systems and popularized in the 1964 Surgeon General’s report *Smoking and Health*,⁷⁶ has been a hallmark of scientific reasoning aimed at assessing evidence in relation to complex causes for more than a half century. The logical flaw in using the FLT to explain secular changes in body weight is reflected in nonadherence to these criteria for judging causality. Specifically, invoking the FLT to explain secular trends in weight gain fails criteria 3, specificity, and 4, temporality. In addition, because of its inability to control for confounding or to estimate effect modification, the FLT provides little useful information for assessing other criteria (ie, the strength of the association, consistency across different sources of evidence, dose-response, plausibility, coherence, and analogy). To illustrate its inability to offer a meaningful explanation of cause, one should consider the analogy of fuel consumption and automobile driving. The average distance driven by motorists has steadily increased since 1980 (in parallel with obesity rates). At the same time, fuel consumption has increased. Although these data are simply and obviously correlated, on their own they do nothing to answer the question: Why are people now driving greater distances? Similarly, to understand the obesity epidemic, we need to search for potentially modifiable root factors that can be

measured and modeled to see how well they fit the criteria for judging causality. We should not be satisfied with tautological statements based on the FLT. The flawed logic that naturally flows from naive appeals to the FLT and EB conjectures (eg, increased caloric intake must lead to increased obesity) has biased research funding decisions and the choice of study designs, operational definitions of variables, choice of measurement methods, and analytic procedures, which all condition higher-level decisions regarding how, when, and where to intervene.

Simplistic Determinism and Reductionism—Reliance on FLT-based models leads to neglecting a potentially large array of complex, dynamic, nonlinear, homeostatic systems (eg, energy metabolism and feeding behavior) in favor of static, deterministic equivalency, an extreme form of reductionism in which the complexity of physiologic features and behavior are reduced to basic physics. More importantly, the manifest assumption of FLT-based models is that energy imbalances, no matter how trivial, lead to linear extrapolations to changes in body mass. Measurement and conceptual issues aside, the fallacy of this a priori assumption is obvious; during the past 50 years, it has been reported repeatedly that biological organisms adapt physiologically, behaviorally, or both to perturbations in EB.^{58,77–80} The effects of acute or chronic changes in any component of the EB equation will be damped via compensatory alterations in EI (ie, feeding behavior) or EE through changes in body composition or PA or some combination of these.^{80,81} In addition, the wealth of responses available to free-living people may well reduce, eliminate, or even reverse the intended effects of any environmental alteration (ie, an intervention).^{82–85} This reality makes policy^{82,85,86} and funding⁵ decisions based on deterministic equivalencies unproductive in that they incentivize research that fails to account for the array of recalibrations and adjustments that free-living people undergo.

Measurement and Introspection—Very little of the literature on which we base inferences is from the strongest of study designs: randomized controlled trials (RCTs).⁸⁷ Likewise, measurement methods commonly used to assess EI and EE lack the accuracy, reliability, and precision necessary to evaluate the efficacy of interventions or even to draw conclusions from carefully designed observational studies when RCTs are infeasible.^{64,69,71–73,88} This also was (and is) true of the relationship between tobacco exposure and health outcomes, to which the criteria for judging causality were most famously applied.⁷⁶ However, those relationships were easier to sort out for 3 reasons: (1) tobacco exposure is easier to measure than diet or PA (or certainly both), (2) tobacco is very strongly associated with the conditions with which it was first associated (eg, lung cancer⁸⁹), and (3) the effect of tobacco is not as heavily confounded by other factors (although effect modification is important for conditions such as esophageal squamous cell cancer^{90,91}).

For diet and PA, true criterion measures (eg, doubly labeled water in carefully controlled settings) rarely exist for practical application in large- or even medium-scale epidemiologic or clinical studies, and even doubly labeled water measurements do not assess an important component of PA: intensity. Consequently, marginal intermethod reliability (between-method correlations of ≈ 0.60 , indicating that 64% of variability is unexplained) is accepted as adequate validity.^{70,92,93} For a variety of practical reasons, observational and even intervention studies rely on inexpensive, inaccurate, and imprecise self-report methods.^{94,95} Construct validation is nearly completely ignored,^{96,97} and methods that could triangulate to objective measures of exposure are rarely used.^{98,99} This satisfaction with inadequate measurement has stunted obesity research and the field of nutritional epidemiology more generally.^{100,101}

Although practical, including financial, constraints must be acknowledged, the scientific community should demand that methodological research be undertaken to improve the

accuracy of self-report, including identifying sources of error with the aim of developing better techniques for statistical adjustment. For example, doubly labeled water (even with its acknowledged weaknesses) could be used to measure EE in carefully controlled intervention studies and could provide a leverage point for improving self-report instruments, as we have done previously.⁷⁰ There are important precedents, most notably from the genetics field, for investing heavily in improved measurement methods and supporting large studies needed to address the complexity of many of the traits under study in human genetics and gene-environment interactions¹⁰² when the potential benefit is perceived to be high in relation to the probable risk from inaction and inattention.

Misuse of Population-Level Data Sources—Numerous data sources are tangential to EI (eg, losses from food inventory and food waste) but are often elevated to causal explanation. Numerous journals have published articles suggesting an invalid determinism (ie, economic forces are not just associated with, but determine, obesity). Although food supply forces (eg, availability and price) may affect purchase and perhaps utilization, the mere presence, purchase, or even increased consumption of food does not necessarily cause long-term changes in adiposity.^{80,81,103–107}

Lack of Due Diligence in Upholding Rigorous Standards of Scientific Evidence When Seemingly Good Ends Are Pursued

Despite that obesity may not simply be the result of overeating,^{80,81,104} numerous journals continue to publish articles suggesting that the superficial economics (eg, mere availability of cheap “junk” food) has *caused* the obesity epidemic.^{108–114} Adherence to assumptions with no factual foundation does little to advance scientific understanding. Obesity is widely portrayed as an evil enemy,^{115,116} and it is commonly accepted that when we are at war and perceive ourselves to be “the good guys,” valid means of collecting and analyzing data are put aside in favor of expedience in doing what it takes to win the war. The resulting bias permeates the larger social/environmental context, influencing peer review of publication, grants, and, perhaps more importantly, upstream decisions to forgo more expensive, intensive research that addresses the nuances of the complexity of the obesity epidemic.

DISCUSSION AND RECOMMENDATIONS

Our inability to materially and durably decrease the population prevalence of obesity or adiposity in targeted individuals is noteworthy.^{8–14} Interventions aimed at increasing EE (eg, through improved physical education classes, incentivizing the use of health clubs/exercise facilities, and adding walking/cycling paths to decrease automobile use and increase human-powered transportation) or decreasing EI (eg, through weight-loss programs, nutrition education, taxing specific food commodities, and food labeling) seem not to result in long-term weight loss, despite appeals to the FLT^{117–122}.

Crude models of obesity have constrained research for decades, from study design choices, selection and measurement of variables, operational definitions, development and use of measurement tools, and decisions as to how, when, and where to intervene. The flawed logic, vague concepts, inaccurate and imprecise measurements, and unsubstantiated a priori assumptions regarding causal relationships that have followed from vague and poorly specified models during the past century have engendered policy and funding decisions that have incentivized research that perpetuates and compounds these errors via confirmation bias while constraining research paths incongruent with prevailing assumptions.

Conjectures emanating from studies based on the current models of obesity coupled with policy and funding decisions that narrowly constrain future inquiry have contributed to a failure of the peer review process to deepen understanding of obesity at all levels of inquiry.

To understand the scope of the problem, we need to remain aware of the fact that obesity arises from the dynamic interplay of the external environment^{43–45} with behavioral and developmental processes^{49,50} and genetic and epigenetic factors.^{51–53} When conceptualized in this manner, it becomes evident that simple, deterministic statements about the etiology of obesity and narrow interpretation about the scope of fundable research are naive and inherently unscientific.¹⁰⁹

Future research should accommodate the apparent complexity of the obesity problem. Conceptualizing a problem implies specification of how to measure and quantify those things that are hypothesized to be important in its cause (or remediation). Because of the narrow interpretation of the causes of the obesity problem, measurement technologies have tended to represent a limited set of possibilities. In planning how to move forward, it is important to consider broadening our interpretation of measurement devices to include study design as an important subset.¹²³ Although RCTs may be a good choice because of the potentially tight control over extraneous factors, it must be realized that often only 1 or 2 factors can be controlled by design. In addition, it is important to appreciate that just because individuals are randomized to a particular study arm in no way guarantees that baseline factors will be entirely equivalent (or exchangeable), that important effect modifiers or confounders will not change differentially over time, that there will be complete adherence, or that there will not be differential dropout.^{124,125} Although these factors would plague even simple pharmacologic interventions, it is reasonable to assume that they might be much more severe in situations in which considerable participant commitment is required and blinding is not possible.

Regardless of the specific design chosen, measurements should include potential adaptive behavioral and physiologic responses to specific changes in EI or EE that may mitigate their expected effects. Usually these adaptive behaviors occur in social contexts that integrate physiologic factors with social cues.^{126,127} Understanding motivational issues regarding food choices^{128–130} and the willingness and ability to engage in a sufficient PA dose (ie, intensity, frequency, and duration) over time^{129,131} also represents an important part of successfully designing studies that will materially improve obesity-related outcomes.

Recognizing that such adaptive behaviors cannot be controlled by design,^{132,133} existing methods for collecting this kind of information can be used across a variety of experimental and observational study designs for broad applicability in advancing and deepening our understanding of the causes and treatments of obesity.^{9,19,21,22,60} Such statistical methods are well described and commonly used in epidemiologic research, in which effect modification and potential confounding are ubiquitous concerns in the analysis of real-world data, whether collected in the context of an RCT or observationally.^{134–136}

It also is important to choose appropriately from the continuum of efficacy and effectiveness study designs.¹³⁷ The use of experimental designs may, indeed, be more appropriate for the study of the causes of obesity, and we would tend to recommend such designs in general.^{138,139} However, note that the actual differences in EI vs EE necessary to cause measurable changes in energy stores tend to be relatively small (ie, just a few extra kilocalories per day can lead to a couple of kilograms of weight gain per year).^{140,141} The fact that even morbidly obese people are in relatively good balance over extended periods of time underlines people's adaptive ability.^{55,80,142} Therefore, compensatory factors that cannot be incorporated as design features of any proposed study must be controlled analytically. This requires anticipating possible mechanisms and either using existing methods or developing new ones to measure these factors and analyze data that are collected using appropriate assessment methods.

To address the public health dimension of the problem, at least some of these studies must be conducted in the context of how people actually lead their lives. Unlike studies of many pharmaceutical agents, behavioral interventions cannot be blinded from the perspective of the participants.^{124,143} Also, there may be ethical issues that either inhibit randomization or cause individuals (eg, the morbidly obese) to refuse to be randomized.^{60,144}

Regarding assessment of the primary exposures, it seems necessary to improve measurement techniques and curtail the use of inaccurate self-reports of diet and PA without identifying methods of adjustment to improve accuracy. We must increase investments in measuring EI and EE more accurately in largescale surveys and epidemiologic studies. Developing more practical objective measurement methods should be a high priority because widely used self-reports are often subject to large sources of measurement bias.¹⁴⁵ Although developing entirely new methods may be desirable, identifying sources of error and then using these data to develop analytic methods to reduce their influence on drawing erroneous inferences might be a desirable interim goal. Rapid progress in developing objective measures of PA that are feasible for use in large-scale studies of free-living individuals is encouraging.¹⁴⁶ Likewise, work that has been conducted on defining sources of measurement error in relation to an “objective” criterionmeasure (eg, doubly labeled water)^{70,147} and then using this information to improve estimation of construct validators (eg, body weight, body composition, and serum lipid levels)^{148,149} holds promise for advancing this field of obesity research.

CONCLUSION

Current rates of obesity and related conditions continue to place unrelenting strain on health care resources and to reduce productivity. If our response is to be commensurate with the seriousness of the problem, the scientific community must demand higher standards in efforts to understand obesity’s causes and potential solutions.

Acknowledgments

Grant Support: Dr Hebert was supported by an Established Investigator Award in Cancer Prevention and Control from the Cancer Training Branch of the National Cancer Institute (K05 CA136975).

Abbreviations and Acronyms

BF	body fat
BMI	body mass index
CHD	coronary heart disease
CVD	cardiovascular disease
EB	energy balance
EE	energy expenditure
EI	energy intake
FLT	first law of thermodynamics
PA	physical activity
RCT	randomized controlled trial

REFERENCES

1. World Health Organization. Mortality and Burden of Disease Estimates for WHO Member States in 2004. Geneva, Switzerland: World Health Organization; 2009.
2. World Health Organization. World Health Statistics. Geneva, Switzerland: World Health Organization; 2010.
3. Beaglehole R, Ebrahim S, Reddy S, Voute J, Leeder S. Chronic Disease Action Group. Prevention of chronic diseases: a call to action. *Lancet*. 2007; 370(9605):2152–2157. [PubMed: 18063026]
4. Beaglehole R, Bonita R, Horton R, et al. Priority actions for the non-communicable disease crisis. *Lancet*. 2011; 377(9775):1438–1447. [PubMed: 21474174]
5. National Institutes of Health. Strategic Plan for NIH Obesity Research: A Report of the NIH Obesity Research Task Force. Washington, DC: US Department of Health and Human Services; 2011 Mar. NIH publication 11-5493
6. Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC). Bethesda, MD: National Institutes of Health; 2013.
7. Andreyeva T, Long MW, Henderson KE, Grode GM. Trying to lose weight: diet strategies among Americans with overweight or obesity in 1996 and 2003. *J Am Diet Assoc*. 2010; 110(4):535–542. [PubMed: 20338279]
8. Kamath CC, Vickers KS, Ehrlich A, et al. Clinical review: behavioral interventions to prevent childhood obesity: a systematic review and metaanalyses of randomized trials. *J Clin Endocrinol Metab*. 2008; 93(12):4606–4615. [PubMed: 18782880]
9. Monasta L, Batty GD, Macaluso A, et al. Interventions for the prevention of overweight and obesity in preschool children: a systematic review of randomized controlled trials. *Obes Rev*. 2011; 12(5):e107–e118. [PubMed: 20576004]
10. Weintraub M. Long-term weight control: the National Heart, Lung, and Blood Institute funded multimodal intervention study. *Clin Pharmacol Ther*. 1992; 51(5):581–585. [PubMed: 1445528]
11. Waseem T, Mogensen KM, Lautz DB, Robinson MK. Pathophysiology of obesity: why surgery remains the most effective treatment. *Obes Surg*. 2007; 17(10):1389–1398. [PubMed: 18000735]
12. Kassirer JP, Angell M. Losing weight: an ill-fated New Year's resolution. *N Engl J Med*. 1998; 338(1):52–54. [PubMed: 9414332]
13. Summerbell CD, Waters E, Edmunds LD, Kelly S, Brown T, Campbell KJ. Interventions for preventing obesity in children. *Cochrane Database Syst Rev*. 2005; (3) CD001871.
14. Franz MJ, VanWormer JJ, Crain AL, et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *J Am Diet Assoc*. 2007; 107(10):1755–1767. [PubMed: 17904936]
15. Gill T, King L, Caterson I. Obesity prevention: necessary and possible: a structured approach for effective planning. *Proc Nutr Soc*. 2005; 64(2):255–261. [PubMed: 15960870]
16. Small, L.; Lane, H.; Vaughan, L.; Melnyk, B.; McBurnet, D. A systematic review of the evidence: the effects of portion size manipulation with children and portion education/training interventions on dietary intake with adults [published online June 15, 2012]. *Worldviews Evid Based Nurs*. <http://dx.doi.org/10.1111/j.1741-6787.2012.00257>
17. de la Hunty A, Gibson S, Ashwell M. Does regular breakfast cereal consumption help children and adolescents stay slimmer? a systematic review and meta-analysis. *Obesity Facts*. 2013; 6(1):70–85. [PubMed: 23466487]
18. Cope MB, Allison DB. White hat bias: a threat to the integrity of scientific reporting. *Acta Paediatr*. 2010; 99(11):1615–1617. [PubMed: 21039822]
19. Casazza K, Fontaine KR, Astrup A, et al. Myths, presumptions, and facts about obesity. *N Engl J Med*. 2013; 368(5):446–454. [PubMed: 23363498]
20. Finkelstein EA, Bilger M. Hard truths and a new strategy for addressing childhood obesity. *Child*. 2012; 8(2):106–109.
21. Sparling PB, Franklin BA, Hill JO. Energy balance: the key to a unified message on diet and physical activity. *J Mol Signal*. 2013; 33(1):12–15.
22. Casazza K, Allison DB. Stagnation in the clinical, community and public health domain of obesity: the need for probative research. *Clin Obes*. 2013; 2(3–4):83–85.

23. Hafekost K, Lawrence D, Mitrou F, O'Sullivan TA, Zubrick SR. Tackling overweight and obesity: does the public health message match the science? *BMC Med.* 2013; 11(1):41. [PubMed: 23414295]
24. Rahman M, Berenson AB. Accuracy of current body mass index obesity classification for white, black, and Hispanic reproductive-age women. *Obstet Gynecol.* 2010; 115(5):982–988. [PubMed: 20410772]
25. Donegan WL, Hartz AJ, Rimm AA. The association of body weight with recurrent cancer of the breast. *Cancer.* 1978; 41(4):1590–1594. [PubMed: 639014]
26. Lubin F, Ruder AM, Wax Y, Modan B. Overweight and changes in weight throughout adult life in breast cancer etiology: a case-control study. *Am J Epidemiol.* 1985; 122(4):579–588. [PubMed: 4025301]
27. McNee RK, Mason BH, Neave LM, Kay RG. Influence of height, weight, and obesity on breast cancer incidence and recurrence in Auckland, New Zealand. *Breast Cancer Res Treat.* 1987; 9(2): 145–150. [PubMed: 3620716]
28. Hebert JR, Augustine A, Barone J, Kabat GC, Kinne DW, Wynder EL. Weight, height and body mass index in the prognosis of breast cancer: early results of a prospective study. *Int J Cancer.* 1988; 42:315–318. [PubMed: 3417358]
29. Boffetta P, McLerran D, Chen Y, et al. Body mass index and diabetes in Asia: a cross-sectional pooled analysis of 900,000 individuals in the Asia cohort consortium. *PLoS One.* 2011; 6(6):e19930. [PubMed: 21731609]
30. Gnacinska M, Malgorzewicz S, Guzek M, Lysiak-Szydłowska W, Sworczak K. Adipose tissue activity in relation to overweight or obesity. *Endokrynol Pol.* 2010; 61(2):160–168. [PubMed: 20464701]
31. Garn SM, Leonard WR, Hawthorne VM. Three limitations of the body mass index. *Am J Clin Nutr.* 1986; 44(6):996–997. [PubMed: 3788846]
32. Gray DS, Fujioka K. Use of relative weight and Body Mass Index for the determination of adiposity. *J Clin Epidemiol.* 1991; 44(6):545–550. [PubMed: 2037859]
33. Van Itallie TB. When the frame is part of the picture. *Am J Public Health.* 1985; 75(9):1054–1055. [PubMed: 4025655]
34. Steinkamp RC, Cohen NL, Gaffey WR, et al. Measures of body fat and related factors in normal adults, II: a simple clinical method to estimate body fat and lean body mass. *J Chronic Dis.* 1965; 18(12):1291–1307. [PubMed: 5852581]
35. Amador M, Rodriguez C, Gonzalez ME, Bacallao J. Assessing obesity with body weight and height. *Acta Paediatr Acad Sci Hung.* 1982; 23(4):381–390. [PubMed: 7170949]
36. Pasco JA, Rutishauser IH. Body fat estimated from anthropometric and electrical impedance measurements. *Hum Nutr Clin Nutr.* 1985; 39(5):365–369. [PubMed: 4055427]
37. Skelton JA, Irby MB, Grzywacz JG, Miller G. Etiologies of obesity in children: nature and nurture. *Pediatr Clin North Am.* 2011; 58(6):1333–1354. ix. [PubMed: 22093854]
38. Thomas EL, Parkinson JR, Frost GS, et al. The missing risk: MRI and MRS phenotyping of abdominal adiposity and ectopic fat. *Obesity.* 2012; 20(1):76–87. [PubMed: 21660078]
39. Hall KD, Heymsfield SB, Kemnitz JW, Klein S, Schoeller DA, Speakman JR. Energy balance and its components: implications for body weight regulation. *Am J Clin Nutr.* 2012; 95(4):989–994. [PubMed: 22434603]
40. Kraemer WJ, Torine JC, Silvestre R, et al. Body size and composition of National Football League players. *J Strength Cond Res.* 2005; 19(3):485–489. [PubMed: 16095394]
41. Heshka S, Allison DB. Is obesity a disease? *Int J Obes Relat Metab Disord.* 2001; 25(10):1401–1404. [PubMed: 11673757]
42. Atkinson, RL. Etiologies of obesity. In: Goldstein, DJ., editor. *The Management of Eating Disorders and Obesity.* Vol. 2. Totowa, NJ: Humana Press; 2005.
43. Klimentidis YC, Beasley TM, Lin HY, et al. Canaries in the coal mine: a cross-species analysis of the plurality of obesity epidemics. *Proc Biol Sci.* 2011; 278(1712):1626–1632. [PubMed: 21106594]

44. Vimalleswaran KS, Li S, Zhao JH, et al. Physical activity attenuates the body mass index-increasing influence of genetic variation in the FTO gene. *Am J Clin Nutr.* 2009; 90(2):425–428. [PubMed: 19553294]
45. Kilpelainen TO, Qi L, Brage S, et al. Physical activity attenuates the influence of FTO variants on obesity risk: a meta-analysis of 218,166 adults and 19,268 children. *PLoS Med.* 2011; 8(11):e1001116.
46. Pinnick KE, Karpe F. DNA methylation of genes in adipose tissue. *Proc Nutr Soc.* 2011; 70(1):57–63. [PubMed: 21144123]
47. Gluckman PD, Hanson MA. Developmental and epigenetic pathways to obesity: an evolutionary-developmental perspective. *Int J Obes (Lond).* 2008; 32:S62–S71. [PubMed: 19136993]
48. Gluckman PD, Hanson MA, Low FM. The role of developmental plasticity and epigenetics in human health. *Birth Defects Res C Embryo Today.* 2011; 93(1):12–18. [PubMed: 21425438]
49. Kimura Y, Nanri A, Matsushita Y, Sasaki S, Mizoue T. Eating behavior in relation to prevalence of overweight among Japanese men. *Asia Pac J Clin Nutr.* 2011; 20(1):29–34. [PubMed: 21393107]
50. Comuzzie AG, Allison DB. The search for human obesity genes. *Science.* 1998; 280(5368):1374–1377. [PubMed: 9603720]
51. Perusse L, Rankinen T, Zuberi A, et al. The human obesity gene map: the 2004 update. *Obes Res.* 2005; 13(3):381–490. [PubMed: 15833932]
52. Blechman J, Amir-Zilberstein L, Gutnick A, Ben-Dor S, Levkowitz G. The metabolic regulator PGC-1 α directly controls the expression of the hypothalamic neuropeptide oxytocin. *J Neurosci.* 2011; 31(42):14835–14840. [PubMed: 22016516]
53. Paracchini V, Pedotti P, Taioli E. Genetics of leptin and obesity: a HuGE review. *Am J Epidemiol.* 2005; 162(2):101–114. [PubMed: 15972940]
54. Reinehr T, Wabitsch M. Childhood obesity. *Curr Opin Lipidol.* 2011; 22(1):21–25. [PubMed: 20871401]
55. Pijl H. Obesity: evolution of a symptom of affluence. *Neth J Med.* 2011; 69(4):159–166. [PubMed: 21527802]
56. Hu FB. Globalization of diabetes: the role of diet, lifestyle, and genes. *Diabetes Care.* 2011; 34(6):1249–1257. [PubMed: 21617109]
57. Nguyen DM, El-Serag HB. The epidemiology of obesity. *Gastroenterol Clin North Am.* 2010; 39(1):1–7. [PubMed: 20202574]
58. Li X, Cope MB, Johnson MS, Smith DL Jr, Nagy TR. Mild calorie restriction induces fat accumulation in female C57BL/6J mice. *Obesity (Silver Spring).* 2010; 18(3):456–462. [PubMed: 19798071]
59. Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight [published correction appears. *N Engl J Med.* 1995; 333(6):399. *N Engl J Med.* 1995;332(10):621–628.
60. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and metaanalysis. *JAMA.* 2013; 309(1):71–82. [PubMed: 23280227]
61. Lavie CJ, De Schutter A, Patel DA, et al. New insights into the “obesity paradox” and cardiovascular outcomes. *J Glycomics Lipidomics.* 2012; 2:e106. <http://dx.doi.org/10.4172/2153-0637.1000e106>.
62. Lavie CJ, De Schutter A, Patel DA, Romero-Corral A, Artham SM, Milani RV. Body composition and survival in stable coronary heart disease: impact of lean mass index and body fat in the “obesity paradox.”. *J Am Coll Cardiol.* 2012; 60(15):1374–1380. [PubMed: 22958953]
63. McAuley PA, Artero EG, Sui X, et al. The obesity paradox, cardiorespiratory fitness, and coronary heart disease. *Mayo Clin Proc.* 2012; 87(5):443–451. [PubMed: 22503065]
64. Lavie CJ, De Schutter A, Patel D, Artham SM, Milani RV. Body composition and coronary heart disease mortality: an obesity or a lean paradox? *Mayo Clin Proc.* 2011; 86(9):857–864. [PubMed: 21878597]
65. Lavie CJ, Cahalin LP, Chase P, et al. Impact of cardiorespiratory fitness on the obesity paradox in patients with heart failure. *Mayo Clin Proc.* 2013; 88(3):251–258. [PubMed: 23489451]

66. Klesges LM, Baranowski T, Beech B, et al. Social desirability bias in self-reported dietary, physical activity and weight concerns measures in 8- to 10-year-old African-American girls: results from the Girls Health Enrichment Multisite Studies (GEMS). *Prev Med.* 2004; 38(suppl):S78–S87. [PubMed: 15072862]
67. Hill RJ, Davies PS. The validity of self-reported energy intake as determined using the doubly labelled water technique. *Br J Nutr.* 2001; 85(4):415–430. [PubMed: 11348556]
68. Schoeller DA. Limitations in the assessment of dietary energy intake by self-report. *Metabolism.* 1995; 44:18–22. [PubMed: 7869932]
69. Black AE, Prentice AM, Goldberg GR, et al. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc.* 1993; 93(5): 572–579. [PubMed: 8315169]
70. Hebert JR, Ebbeling CB, Matthews CE, et al. Systematic errors in middle-aged women's estimates of energy intake: comparing three self-report measures to total energy expenditure from doubly labeled water. *Ann Epidemiol.* 2002; 12:577–586. [PubMed: 12495831]
71. Wong MY, Day NE, Wareham NJ. Measurement error in epidemiology: the design of validation studies, II: bivariate situation. *Stat Med.* 1999; 18(21):2831–2845. [PubMed: 10523745]
72. Wareham NJ, Jakes RW, Rennie KL, Mitchell J, Hennings S, Day NE. Validity and repeatability of the EPIC-Norfolk Physical Activity Questionnaire. *Int J Epidemiol.* 2002; 31(1):168–174. [PubMed: 11914316]
73. Westterterp KR, Plasqui G. Physical activity and human energy expenditure. *Curr Opin Clin Nutr Metab Care.* 2004; 7(6):607–613. [PubMed: 15534427]
74. Hill AB. Observation and experiment. *N Engl J Med.* 1953; 248:3–9.
75. Hill AB. The environment and disease: association or causation? *Proc R Soc Med.* 1965; 58:295–300. [PubMed: 14283879]
76. US Department of Health, Education, and Welfare. Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Services. Washington, DC: Public Health Service; 1964. PHS publication 1103
77. Keys, A.; Brozek, J.; Henschel, A.; Mickelsen, O.; Taylor, HL. *The Biology of Human Starvation.* Minneapolis, MN: University of Minnesota Press; 1950.
78. Mayer J, Marshall NB, Vitale JJ, Christensen JH, Mashayekhi MB, Stare FJ. Exercise, food intake and body weight in normal rats and genetically obese adult mice. *Am J Physiol.* 1954; 177(3):544–548. [PubMed: 13158612]
79. Sullivan EL, Cameron JL. A rapidly occurring compensatory decrease in physical activity counteracts diet-induced weight loss in female monkeys. *Am J Physiol Regul Integr Comp Physiol.* 2010; 298(4):R1068–R1074. [PubMed: 20071608]
80. Hall KD. Predicting metabolic adaptation, body weight change, and energy intake in humans. *Am J Physiol Endocrinol Metab.* 2011; 298(3):E449–E466. [PubMed: 19934407]
81. Hall KD, Sacks G, Chandramohan D, et al. Quantification of the effect of energy imbalance on bodyweight. *Lancet.* 2011; 378(9793):826–837. [PubMed: 21872751]
82. Edwards R. Sugar-sweetened beverage taxes raise demand for substitutes and could even raise caloric intake. *Prev Med.* 2012; 54(3–4):284–285.
83. Harris KC, Kuramoto LK, Schulzer M, Retallack JE. Effect of school-based physical activity interventions on body mass index in children: a meta-analysis. *CMAJ.* 2009; 180(7):719–726. [PubMed: 19332753]
84. Faith MS, Fontaine KR, Baskin ML, Allison DB. Toward the reduction of population obesity: macrolevel environmental approaches to the problems of food, eating, and obesity. *Psychol Bull.* 2007; 133(2):205–226. [PubMed: 17338597]
85. Taber DR, Chriqui JF, Powell LM, Chaloupka FJ. Banning all sugar-sweetened beverages in middle schools: reduction of in-school access and purchasing but not overall consumption. *Arch Pediatr Adolesc Med.* 2012; 166(3):256–262. [PubMed: 22064875]
86. Lin BH, Smith TA, Lee JY, Hall KD. Measuring weight outcomes for obesity intervention strategies: the case of a sugarsweetened beverage tax. *Econ Hum Biol.* 2011; 9(4):329–341. [PubMed: 21940223]

87. Allison DB. Evidence, discourse and values in obesity-oriented policy: menu labeling as a conversation starter. *Int J Obes*. 2011; 35(4):464–471.
88. Hebert JR, Ma Y, Clemow L, et al. Gender differences in social desirability and social approval bias in dietary self report. *Am J Epidemiol*. 1997; 146(12):1046–1055. [PubMed: 9420529]
89. Wynder EL, Graham EA. Tobacco smoking as a possible etio-logic factor in bronchogenic carcinoma: a study of six hundred and eighty-four proved cases. *JAMA*. 1950; 143(4):329–336.
90. Pottern LM, Morris LE, Blot WJ, Ziegler RG, Fraumeni JF Jr. Esophageal cancer among black men in Washington, D.C., I: alcohol, tobacco, and other risk factors. *J Natl Cancer Inst*. 1981; 67(4):777–783. [PubMed: 6944547]
91. Yuan J-M, Knezevich AD, Wang R, Gao Y-T, Hecht SS, Stepanov I. Urinary levels of the tobacco-specific carcinogen N'-nitrosornicotine and its glucuronide are strongly associated with esophageal cancer risk in smokers. *Carcinogenesis*. 2011; 32(9):1366–1371. [PubMed: 21734256]
92. Kaaks R, Ferrari P, Ciampi A, Plummer M, Riboli E. Uses and limitations of statistical accounting for random error correlations, in the validation of dietary questionnaire assessments. *Public Health Nutr*. 2002; 5(6A):969–976. [PubMed: 12638598]
93. Neuhouser ML, Tinker L, Shaw PA, et al. Use of recovery bio-markers to calibrate nutrient consumption self-reports in the Women's Health Initiative. *Am J Epidemiol*. 2008; 167(10):1247–1259. [PubMed: 18344516]
94. Oza-Frank R, Cheng YJ, Narayan KM, Gregg EW. Trends in nutrient intake among adults with diabetes in the United States: 1988–2004. *J Am Diet Assoc*. 2009; 109(7):1173–1178. [PubMed: 19559133]
95. Hebert, JR.; Ma, Y.; Ebbeling, CB.; Matthews, CE.; Ockene, IS. Self-report data. In: Ockene, IS.; Burke, LE., editors. *Compliance in Healthcare and Research*. Armonk, NY: Futura; 2001. p. 163-179.
96. Hebert JR, Ockene IS, Hurley TG, Luippold R, Well AD, Harmatz MG. Dietary Assessment Working Group of the Worcester Area Trial for Counseling in Hyperlipidemia (WATCH). Development and testing of a seven-day dietary recall. *J Clin Epidemiol*. 1997; 50(8):925–937. [PubMed: 9291878]
97. Ockene IS, Hebert JR, Ockene JK, et al. Effect of physician-delivered nutrition counseling training and an office support system on saturated fat intake, weight, and serum lipid measurements in a hyperlipidemic population: the Worcester-Area Trial for Counseling in Hyperlipidemia (WATCH). *Arch Intern Med*. 1999; 159(7):725–731. [PubMed: 10218753]
98. Fowke JH, Hebert JR, Fahey JW. Urinary excretion of dithio-carbamates and self-reported *Cruciferous* vegetable intake: application of the “method of triads” to a food-specific biomarker. *Public Health Nutr*. 2002; 5(6):791–799. [PubMed: 12570887]
99. Kabagambe EK, Baylin A, Allan DA, Siles X, Spiegelman D, Campos H. Application of the method of triads to evaluate the performance of food frequency questionnaires and bio-markers as indicators of long-term dietary intake. *Am J Epidemiol*. 2001; 154(12):1126–1235. [PubMed: 11744518]
100. Taubes G. What if it's all been a big fat lie? *New York Times Magazine*. 2002 Jul 7.:22–27. 34, 45, 47.
101. Taubes G. The soft science of dietary fat. *Science*. 2001; 291:2536–2545. [PubMed: 11286266]
102. Li S, Loos RJF. Progress in the genetics of common obesity: size matters. *Curr Opin Lipidol*. 2008; 19(2):113–121. [PubMed: 18388690]
103. Matsumura Y. Nutrition trends in Japan. *Asia Pac J Clin Nutr*. 2001; 10(suppl):S40–S47. [PubMed: 11708582]
104. Sims EA, Danforth E Jr, Horton ES, Bray GA, Glennon JA, Salans LB. Endocrine and metabolic effects of experimental obesity in man. *Recent Prog Horm Res*. 1973; 29:457–496. [PubMed: 4750591]
105. Speakman JR. Obesity: the integrated roles of environment and genetics. *J Nutr*. 2004; 134(8, suppl):2090S–2105S. [PubMed: 15284410]
106. Speakman JR, Stubbs RJ, Mercer JG. Does body mass play a role in the regulation of food intake? *Proc Nutr Soc*. 2002; 61(4):473–487. [PubMed: 12691177]

107. Katanoda K, Matsumura Y. National Nutrition Survey in Japan: its methodological transition and current findings. *J Nutr Sci Vitaminol (Tokyo)*. 2002; 48(5):423–432. [PubMed: 12656220]
108. Poti JM, Popkin BM. Trends in energy intake among US children by eating location and food source, 1977–2006. *J Am Diet Assoc*. 2011; 111(8):1156–1164. [PubMed: 21802561]
109. Swinburn B, Sacks G, Ravussin E. Increased food energy supply is more than sufficient to explain the US epidemic of obesity. *Am J Clin Nutr*. 2009; 90(6):1453–1456. [PubMed: 19828708]
110. Swinburn BA, Sacks G, Lo SK, et al. Estimating the changes in energy flux that characterize the rise in obesity prevalence. *Am J Clin Nutr*. 2009; 89(6):1723–1728. [PubMed: 19369382]
111. Duffey KJ, Popkin BM. Energy density, portion size, and eating occasions: contributions to increased energy intake in the United States, 1977–2006. *PLoS Med*. 2011; 8(6) e1001050.
112. Swinburn BA, Sacks G, Hall KD, et al. The global obesity pandemic: shaped by global drivers and local environments. *Lancet*. 2011; 378(9793):804–814. [PubMed: 21872749]
113. Swinburn B. Nutrition signposting: the “eat more” message is getting through; what about the “eat less” message? *Public Health Nutr*. 2012; 15(3):483–485. [PubMed: 21859506]
114. Gortmaker SL, Swinburn BA, Levy D, et al. Changing the future of obesity: science, policy, and action. *Lancet*. 2011; 378(9793):838–847. [PubMed: 21872752]
115. Gluckman PD, Hanson M, Zimmet P, Forrester T. Losing the war against obesity: the need for a developmental perspective. *Sci Transl Med*. 2011; 3(93) 93cm19.
116. Klein JD, Dietz W. Childhood obesity: the new tobacco. *Health Aff (Millwood)*. 2010; 29(3): 388–392. [PubMed: 20194977]
117. Schoeller DA. The energy balance equation: looking back and looking forward are two very different views. *Nutr Rev*. 2009; 67(5):249–254. [PubMed: 19386028]
118. Brown T, Summerbell C. Systematic review of school-based interventions that focus on changing dietary intake and physical activity levels to prevent childhood obesity: an update to the obesity guidance produced by the National Institute for Health and Clinical Excellence. *Obes Rev*. 2009; 10(1):110–141. [PubMed: 18673306]
119. Wilks DC, Besson H, Lindroos AK, Ekelund U. Objectively measured physical activity and obesity prevention in children, adolescents and adults: a systematic review of prospective studies. *Obes Rev*. 2011; 12(5):e119–e129. [PubMed: 20604868]
120. Pinelli L, Elerdini N, Faith MS, et al. Childhood obesity: results of a multicenter study of obesity treatment in Italy. *J Pediatr Endocrinol Metab*. 1999; 12(suppl 3):795–799. [PubMed: 10626272]
121. Corvalan C, Uauy R, Flores R, Kleinbaum D, Martorell R. Reductions in the energy content of meals served in the Chilean National Nursery School Council Program did not consistently decrease obesity among beneficiaries. *J Nutr*. 2008; 138(11):2237–2243. [PubMed: 18936225]
122. Foster GD, Sherman S, Borradaile KE, et al. A policy-based school intervention to prevent overweight and obesity. *Pediatrics*. 2008; 121(4):e794–e802. [PubMed: 18381508]
123. Miettinen, OS. *Theoretical Epidemiology: Principles of Occurrence Research in Medicine*. New York, NY: John Wiley & Sons Inc; 1985.
124. Hebert JR, Hurley TG, Harmon BE, Heiney S, Hebert CJ, Steck SE. A diet, physical activity, and stress reduction intervention in men with rising prostate-specific antigen after treatment for prostate cancer. *Cancer Epidemiol*. 2012; 36(2):e128–e136. [PubMed: 22018935]
125. Lodi G, Sardella A, Bez C, Demarosi F, Carrassi A. Systematic review of randomized trials for the treatment of oral leukoplakia. *J Dent Educ*. 2002; 66(8):896–902. [PubMed: 12214837]
126. Lundberg PC, Thrakul S. Type 2 diabetes: how do Thai Buddhist people with diabetes practise self-management? *J Adv Nurs*. 2012; 68(3):550–558. [PubMed: 21711465]
127. Steptoe A, Dockray S, Wardle J. Positive affect and psychobiological processes relevant to health. *J Pers*. 2009; 77(6):1747–1776. [PubMed: 19796062]
128. Goldberg JP, Sliwa SA. Communicating actionable nutrition messages: challenges and opportunities. *Proc Nutr Soc*. 2011; 70(1):26–37. [PubMed: 21208498]
129. Kuk JL, Ardern CI, Church TS, Hebert JR, Sui X, Blair SN. Ideal weight and weight satisfaction: association with health practices. *Am J Epidemiol*. 2009; 170(4):456–463. [PubMed: 19546153]

130. Narchi I, Walrand S, Boirie Y, Rousset S. Emotions generated by food in elderly French people. *J Nutr Health Aging*. 2008; 12(9):626–633. [PubMed: 18953460]
131. Yap TL, Davis LS. Physical activity: the science of health promotion through tailored messages. *Rehabil Nurs*. 2008; 33(2):55–62. [PubMed: 18330383]
132. Friedenreich CM, Thune I, Brinton LA, Albanes D. Epidemio-logic issues related to the association between physical activity and breast cancer. *Cancer*. 1998; 83(3, suppl):600–610. [PubMed: 9690523]
133. Prentice RL, Kakar F, Hursting S, Sheppard L, Klein R, Kushi LH. Aspects of the rationale for the Women’s Health Trial. *J Natl Cancer Inst*. 1988; 80(11):802–814. [PubMed: 3292773]
134. Heroux M, Janssen I, Lam M, et al. Dietary patterns and the risk of mortality: impact of cardiorespiratory fitness. *Int J Epidemiol*. 2010; 39(1):197–209. [PubMed: 19380370]
135. Ali MM, Fang H, Rizzo JA. Body weight, self-perception and mental health outcomes among adolescents. *J Ment Health Policy Econ*. 2010; 13(2):53–63. [PubMed: 20919592]
136. Fraser GE. A search for truth in dietary epidemiology. *Am J Clin Nutr*. 2003; 78(3, suppl):521S–525S. [PubMed: 12936944]
137. Stevens J, Taber DR, Murray DM, Ward DS. Advances and controversies in the design of obesity prevention trials. *Obesity*. 2007; 15(9):2163–2170. [PubMed: 17890483]
138. Mattes RD, Shikany JM, Kaiser KA, Allison DB. Nutritively sweetened beverage consumption and body weight: a systematic review and meta-analysis of randomized experiments. *Obes Rev*. 2011; 12(5):346–365. [PubMed: 20524996]
139. Elobeid MA, Allison DB. Putative environmental-endocrine disruptors and obesity: a review. *Curr Opin Endocrinol Diabetes Obes*. 2008; 15(5):403–408. [PubMed: 18769210]
140. Blundell JE, Stubbs RJ, Hughes DA, Whybrow S, King NA. Cross talk between physical activity and appetite control: does physical activity stimulate appetite? *Proc Nutr Soc*. 2003; 62(3):651–661. [PubMed: 14692601]
141. Moore MS. Interactions between physical activity and diet in the regulation of body weight. *Proc Nutr Soc*. 2000; 59(2):193–198. [PubMed: 10946787]
142. Rogers PJ. Eating habits and appetite control: a psychobiological perspective. *Proc Nutr Soc*. 1999; 58(1):59–67. [PubMed: 10343341]
143. Demark-Wahnefried W, Clipp EC, Lipkus IM, et al. Main outcomes of the FRESH START trial: a sequentially tailored, diet and exercise mailed print intervention among breast and prostate cancer survivors. *J Clin Oncol*. 2007; 25(19):2709–2718. [PubMed: 17602076]
144. Ellis PM. Attitudes towards and participation in randomised clinical trials in oncology: a review of the literature. *Ann Oncol*. 2000; 11(8):939–945. [PubMed: 11038029]
145. Freudenheim JL, Marshall JR. The problem of profound mismeasurement and the power of epidemiological studies of diet and cancer. *Nutr Cancer*. 1988; 11:243–250. [PubMed: 3217262]
146. Freedson P, Bowles HR, Troiano R, Haskell W. Assessment of physical activity using wearable monitors: recommendations for monitor calibration and use in the field. *Med Sci Sports Exerc*. 2012; 44(1, suppl 1):S1–S4. [PubMed: 22157769]
147. Adams SA, Matthews CE, Ebbeling CB, et al. The effect of social desirability and social approval on self-reports of physical activity. *Am J Epidemiol*. 2005; 161(4):389–398. [PubMed: 15692083]
148. Hebert JR, Ebbeling CB, Ockene IS, et al. A dietitian-delivered group nutrition program leads to reductions in dietary fat, serum cholesterol, and body weight: findings from the Worcester Area Trial for Counseling in Hyperlipidemia (WATCH). *J Am Diet Assoc*. 1999; 99:544–552. [PubMed: 10333775]
149. Hebert JR, Ebbeling CB, Olendzki BC, et al. Change in women’s diet and body mass following intensive intervention in earlystage breast cancer. *J Am Diet Assoc*. 2001; 101(4):421–431. [PubMed: 11320947]

TABLE 1

The Obesity Pandemic: Major Issues in Scientific and Policy Decision Making

Lack of conceptual clarity

- The conflation of the definition of obesity and classification of the obese phenotype
- Definitions of obesity that vary by discipline
 - Epidemiologic and medical: BMI or waist circumference
 - Physiologic: body fat mass or relative body fat percentage

Imprecise measurement

- The use of BMI at the population level, although imprecise, is above all practical and acceptable. However, its use at the individual level in obesity interventions is inherently misleading owing to the conflation of body mass with fat mass
- The storage of energy occurs at the tissue level, yet the measurement and analyses of changes in body mass, fat mass, and adiposity in people examine changes that sum the effect of tissue-level changes across the entire organism and, therefore, cannot distinguish these specific effects

Obesity paradox

- Confirmation biases plague research in which the a priori assumption is that obesity is on the causal pathway to many health outcomes (eg, CVD, diabetes)
- This has led to paradoxes in which, for example, individuals with higher BMIs have better prognoses (eg, cancer, CVD)

Inferring causality

- The FLT posits that imbalances between energy intake and energy expenditure invariably lead to alterations in energy storage. Nevertheless, the imprecision of many current measurement protocols renders energy balance a conceptual trap rather than a practical model for understanding obesity and pathologic abnormalities in energy storage
- Simplistic notions derived from the FLT have led to numerous naive speculations regarding the obesity pandemic and interventions that ignore physiologic and behavioral compensation (eg, physical education or removal of vending machines will decrease obesity)

Responsibilities of the scientific community

- The peer review process has failed to curtail the publication of speculations that are conceptually tenuous or devoid of empirical support. For example, if increased food availability was a sufficient cause of obesity, entire populations in developed nations would be obese
- Lack of due diligence by the research community has facilitated the publication of studies in which vague and imprecise methods have led to results that are suggestive of multiple and divergent explanations

BMI = body mass index; CVD = cardiovascular disease; FLT = first law of thermodynamics.

TABLE 2

Propagation of Unproven or Even Disproven Propositions as Though They Are Facts^{a,b}

Factor facilitating propagation of presumptions and myths	Example of presumptions erroneously accepted as fact that seem to be facilitated by the factor in column 1	Example of myths erroneously accepted as fact that seem to be facilitated by the factor in column 1
Failure to conduct the probative studies (typically RCTs with weight or body fat as outcomes and sufficient durations to test postulated effects on body composition) needed to prove or disprove hypothesized effects	Regularly eating (vs skipping) breakfast is protective against obesity	NA; things typically can become myths only after probative studies are done
A resistance to abandoning cherished ideas even when refuting data exist (ie, cognitive dissonance)	Early childhood is the period during which we learn exercise and eating habits that influence our weight throughout life	Breastfeeding is protective against obesity for the breastfed offspring
Excessive repetitive presentation of the idea (often on the basis of gratuitous association studies long after they are needed) to the point at which the idea comes to be believed merely by the excessive repetition (ie, the mere exposure effect)	Eating more fruits and vegetables will result in weight loss or less weight gain, regardless of whether one intentionally makes any other behavioral or environmental changes	Large, rapid weight loss is associated with poorer long-term weight outcomes than is slow, gradual weight loss
Failure to ask for supporting data from some ideas that seem intuitively obvious	Preventing obesity is easier than treating obesity ¹⁵	Assessing the stage of change or diet readiness is important in helping patients who seek weight-loss treatment AND Setting realistic goals in obesity treatment is important because otherwise patients will become frustrated and lose less weight
Failure to take into account the passive compensation in energy expenditure that occurs merely as a function of changes in body size that occur with initial alterations in energy intake or expenditure	NA; the passive compensation is an established fact, so any calculations that do not accommodate it are effectively myths, not presumptions	Small, sustained changes in energy intake or expenditure will produce large, long-term weight changes that accumulate indefinitely, which fails to take into account compensatory mechanisms
Failure to take into account the active compensation in components of energy balance that may occur when another component of energy balance is manipulated	Snacking contributes to weight gain and obesity	Physical education classes in their current format play an important role in preventing or reducing childhood obesity
Failure to take into account that the active compensation (or lack thereof) in components of energy expenditure that occurs when another component of energy balance is manipulated over a short period (eg, 1 d) may not be maintained if the manipulation is maintained over a longer period; ie, there may be learned compensation	Reducing portion size in some sources of food will reduce body weight or lead to less weight gain in the long-term ¹⁶	NA
Distortion of the existing scientific evidence by publication and reporting biases or misleading statements	Regularly eating (vs skipping) breakfast is protective against obesity ¹⁷	Breastfeeding is protective against obesity for the breastfed offspring ¹⁸

^aNA = not applicable; RCT = randomized controlled trial.

^bData from *N Engl J Med*¹⁹ References are given only for ideas we classified as myths or presumptions that were not covered by Casazza et al.¹⁹