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Review

Thirty Obesity Myths, Misunderstandings, and/or Oversimplifications: An Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) 2022

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ABSTRACT

Background: This Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) is intended to provide clinicians an overview of 30 common obesity myths, misunderstandings, and/or oversimplifications.
Methods: The scientific support for this CPS is based upon published citations, clinical perspectives of OMA authors, and peer review by the Obesity Medicine Association leadership.
Results: This CPS discusses 30 common obesity myths, misunderstandings, and/or oversimplifications, utilizing referenced scientific publications such as the integrative use of other published OMA CPSs to help explain the applicable physiology/pathophysiology.
Conclusions: This Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) on 30 common obesity myths, misunderstandings, and/or oversimplifications is one of a series of OMA CPSs designed to assist clinicians in the care of patients with the disease of obesity. Knowledge of the underlying science may assist the obesity medicine clinician improve the care of patients with obesity.

1. Introduction

Beginning in 2013, the Obesity Medicine Association (OMA) created and maintained an online Adult "Obesity Algorithm" (i.e., educational slides and eBook) that underwent yearly updates by OMA authors and was reviewed and approved annually by the OMA Board of Trustees [1]. This was followed by a similar Pediatric "Obesity Algorithm" with updates approximately every two years by OMA authors. This current OMA CPS regarding common obesity myths, misunderstandings, and/or overcomplications was largely derived from the 2021 OMA Adult Obesity Algorithm and is one of a series of OMA CPSs designed to assist clinicians in the care of their patients with the disease of obesity.

2. Background

A myth is a commonly held, but inaccurate belief. This CPS discusses the physiology and pathophysiology of 30 common obesity "myths." Many of these 30 items are more accurately characterized as misunderstandings and/or oversimplifications, rather than inaccurate beliefs. A caveat is that some patients and/or clinicians may not agree that all of these are "myths," inaccurate, or even potentially misleading. This may be due to variances in:

- Individual experiences
- Clinical practice experiences
- Differences of interpretation of existing science
- Emergence of new science
- Business interests
- Cultural norms or other global beliefs

This OMA CPS will not be addressing the "obesity paradox," as this is a topic of a forthcoming dedicated OMA CPS entitled: "Cardiovascular Disease, Obesity, and the Obesity Paradox: An Obesity Medicine Association (OMA) Clinical Practice Statement (CPS)." Table 1 lists 30 common "myths" about obesity, each which are discussed in detail in subsequent text sections.

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Table 1
Common Obesity Myths, Misunderstandings, and/or Oversimplifications (MMO).

GENERAL PRINCIPLES	
1.	Obesity is a lifestyle choice and not a disease.
2.	An increase in body weight is always due to an increase in body fat; those with decreased muscle and normal body weight do not develop complications of obesity.
3.	A large amount of weight reduction is required for health benefits.
4.	Weight reduction is difficult; maintaining weight reduction is easy once the weight is lost.
5.	In patients with obesity, increased body fat is the cause of all their health conditions.
6.	People are predestined towards obesity due to an unalterable "setpoint."
7.	Most people with increased body fat are generally healthy and will remain healthy.
ETIOLOGY	
8.	Obesity is mostly due to a defined genetic abnormality.
9.	In the absence of a genetic or secondary medical cause, obesity is mostly due to a lack of willpower.
10.	Obesity is solely caused by eating too much.
11.	Obesity is unrelated to the caloric content of food.
12.	Obesity is caused by eating processed foods.
13.	Obesity is caused by breakfast patterns.
14.	Obesity is commonly caused by pathogens in the intestine (microbiome).
15.	Obesity is due to a lack of access to plant-based foods.
16.	Lack of breastfeeding for a full 2 years is a major sole cause of unalterable obesity in offspring.
DIAGNOSIS	
17.	Increased subcutaneous adipose tissue is healthy; increased visceral adipose tissue is unhealthy.
18.	Individuals with obesity have low metabolism. Lean people are "naturally skinny" because they have a higher metabolism.
19.	"Big boned" individuals have no potential to achieve a healthy body weight.
TREATMENT	
20.	Low fat diets are the best way to reduce body fat.
21.	Nutrition medical therapy is more effective when based upon patient preference.
22.	Vitamins and herbal supplements are effective in achieving weight reduction.
23.	After implementing a 500 Calorie daily energy deficit diet, then as long as this daily energy deficit is maintained, fat weight reduction will continue to occur indefinitely according to the calculation that 3500 Calories are stored per pound of fat.
24.	Increased physical exercise is the most effective way to reduce body weight.
25.	Every pound of muscle that replaces fat burns an additional 50 Calories per day.
26.	Access to exercise equipment, gym memberships, and physical activity trackers will result in weight reduction.
27.	Setting more "realistic" obesity goals will ultimately achieve greater weight reduction than more aggressive goals.
28.	Small favorable changes in nutritional intake and physical activity will yield large long-term benefits; slow and gradual weight reduction is ultimately more effective than large and rapid weight reduction.
29.	Efforts to reduce body weight in patients with obesity is unhealthy, because the weight will inevitably return, and fluctuations in body weight (e.g., yo-yo dieting) are more dangerous than maintaining a high body weight.
30.	Drugs should not be used to treat obesity, because obesity is due to unhealthful diet and lack of exercise, and because weight will only be regained once anti-obesity medications are discontinued. Bariatric surgery is the "easy way out," a procedure reserved for patients who are failures and "cheaters," and is a procedure too dangerous for everyone else.

Listed are 30 common myths, misunderstandings, and/or oversimplifications about obesity.

3. Obesity myths misunderstandings, and/or oversimplifications (MMO)

The discussion of this OMA CPS is focused on obesity:

- General principles
- Etiology
- Diagnosis
- Treatment.

3.1. General principles

3.1.1. ***MMO #1**: obesity is a lifestyle choice and not a disease*

The reason this statement is a myth, misunderstanding, and/or oversimplification is because a "disease" can be defined as adverse anatomic changes to, and/or dysfunction of, an organ or system of the body that results from genetic or development errors, inflammation or infection, poisons, toxicity, nutritional abnormalities, or unfavorable environmental factors that manifest as illness, sickness, or ailment. The signs, symptoms, and pathophysiology of obesity fulfill each of these disease-defining criteria [2] (See Table 2.). The Obesity Medicine Association has defined obesity as:

> *A chronic, progressive, relapsing, and treatable multi-factorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences [3].*

Considerations of obesity as a disease include:

- Positive caloric balance often leads to anatomic enlargement of adipocytes and increased adipose tissue expansion that in addition to promotion of "fat mass disease" (e.g., sleep apnea, orthopedic abnormalities impairing mobility, skin friction), also results in adipocyte and adipose tissue dysfunction (adiposopathy), whose immunopathies and endocrinopathies contribute to the most common metabolic disorders managed in clinical practice (e.g., elevated blood sugar, elevated blood pressure, increase in atherogenic lipoproteins, cardiovascular disease, and cancer) [3–5].

Table 2
Obesity as a disease checklist.

Disease criteria	Obesity
Diagnosed by:	
• Signs and symptoms of illness, sickness, or ailment	✓
• Adverse anatomic changes to an organ or system of the body	✓
• Dysfunction of an organ or system of the body	✓
Contributes to:	
• Increased morbidity	✓
• Increased mortality	✓
Caused by:	
• Genetic or development errors	✓
• Inflammation or infection	✓
• Poisons, toxicity, or adverse side effect of pharmaceuticals	✓
• Nutritional abnormalities	✓
• Unfavorable environmental or behavioral factors	✓
Treated by:	
• Medical nutrition therapy	✓
• Routine physical activity	✓
• Behavior modification	✓
• Medication	✓
• Surgery	✓
• Patient education and training	✓
Managed by:	✓
• Primary care clinicians	✓
• Specialists	✓
• Multidisciplinary team	✓

Obesity meets the criteria as a disease. (See text for detailed description.)

- Obesity can be caused by genetic or epigenetic abnormalities, hypothalamic disorders (including hypothalamic inflammation) [6], insulinoma, some cases of hypothyroidism, hypercortisolism, sleep disorders, microbiota and the microbiome [7–9], consumption of ultra-processed energy dense foods, as well as unhealthful nutrition in an obesogenic environment of physical inactivity and suboptimal education contributing to unhealthful behavior [10,11].
- Obesity can be caused by adverse ("toxic") adverse side effects of concomitant medications [12] as well as obesogens, which are environmental chemicals ("poisons") that promote obesity by disrupting adipose tissue function and/or altering metabolic set points or altering the hormonal regulation of appetite and satiety. Many obesogens are endocrine disrupting chemicals that interfere with normal endocrine regulation [13,14].
- Obesity is a major cause of cardiovascular disease and cancer (i.e., the most common causes of mortality in developed nations) [5], sleep apnea, and numerous other complications of "sick fat" (adiposopathy) and fat mass diseases [3].
- Obesity shares many of the same pathogenic processes as aging [3]. The more advanced age, the greater the mortality. Similarly, the greater the obesity, the greater the mortality. In one example, ~14 years of life is lost for patients with BMI 55–60 kg/m^2, mainly due to the complications of heart disease, cancer, and diabetes mellitus [15].

People do not "choose" to have the disease of obesity, nor is obesity simply a "comorbidity" or "risk factor" regarding its well-known complications. To the extent that "choice" is applicable, this largely depends upon access to education, knowledge, availability of treatment options [11], and choice architecture (i.e., environmental designs involving access to healthful alternatives, and exposure to nutritional and physical activity options in a manner that favorably influences behavior) [16].

3.1.2. ***MMO #2:*** *an increase in body weight is always due to an increase in body fat: those with decreased muscle and normal body weights do not develop complications of obesity*

A body mass index (BMI) ≥ 25 kg/m^2 is generally considered overweight and BMI ≥30 kg/m^2 is considered diagnostic for obesity [3]. While BMI is a reasonable measure for the general adult population, BMI may not accurately measure body composition for the individual. BMI has limitations in assessing adiposity in those with increased muscle mass (i.e., body builders) and those with decreased muscle mass (i.e., sarcopenia), as well as regarding those of different races, different sexes, and pre-versus postmenopausal status [8,17]. Patients with increased muscle mass may have a high BMI and not necessarily have an increase in percent body fat. Unless associated with increased body fat, patients with increased muscle mass do not have an increased risk of cardiovascular disease risk factors such as type 2 diabetes mellitus [18] and hypertension [19,20], nor an increased risk of cardiovascular disease [21] and cancer [21]. Conversely, some patients with reduced muscle mass may have a BMI in the normal range, but increased percent body fat, sometimes termed sarcopenic obesity. Patients with sarcopenic obesity have increased risk of hypertension [22] and diabetes mellitus [23], as well as increased risk of cardiovascular disease [22] and cancer [24].

The amount of fat and muscle in an individual is best evaluated via body composition analyses. Methods to assess body composition vary regarding accuracy, reproducibility, expense, and accessibility [8]. Percent body fat mass is dependent upon both fat mass and lean body mass (i.e., lean body mass includes muscle mass and other non-adipose tissue body organs). From a body fat standpoint, common fat assessment metrics include percent body fat, android fat, and visceral fat. The OMA has suggested that optimal android and visceral fat are <3 pounds and <1 pound, respectively [8]. Percent body fat mass is highly variable among individuals and may range from <5% to >70%. Table 3 describes the OMA categorical descriptions based upon percent body fat, which has applicability to adiposopathic metabolic and inflammatory consequences that help define obesity as a disease [3,4].

Table 3
Obesity medicine association (OMA) classifications of percent body Fat [8].

	Female	Male
Essential fat	<15%	<10%
Athlete	15–19%	10–14%
Fitness	20–24%	15–19%
Acceptable	25–29%	20–24%
Pre-obesity	30–34%	25–29%
Obesity	≥35%	≥30%

For the individual, body composition analyses more accurately measure body fat compared to body mass index (BMI), the OMA has identified the category of "pre-obesity" based upon percent body fat criteria (i.e., not BMI criteria).

3.1.3. ***MMO #3:*** *A large amount of weight reduction is required for health benefits*

Among patients with obesity, current clinical data suggest that larger amounts of weight reduction are required for clinically meaningful improvement in certain health outcomes (e.g., sleep apnea, non-alcoholic steatohepatitis, and cardiovascular and overall mortality outcomes). However, many health benefits can be achieved with >2.5% weight reduction (See Table 4). Most of the benefits in health outcomes with modest weight reduction are due to correction of the adipose tissue endocrine and immune dysfunctions found with obesity. This may be expected, given that 5% weight reduction might not only improve the function of insulin sensitivity in muscle, reduce fat content in liver, and improve pancreatic beta cell function, but also improve multiple aspects of adipocyte and adipose tissue function [25]. This has clinical implications given that increased body fat resulting in adiposopathy (i.e., fat dysfunction) is a major contributor to the most common metabolic abnormalities encountered in clinical practice [3,4].

3.1.4. ***MMO #4:*** *weight reduction is difficult; maintaining weight reduction is easy once the weight is lost*

A common patient claim is: *"If I could just get the weight off, then I know I could keep it off."* Many interventions are successful in facilitating initial weight reduction. While highly variable among individuals, many current non-surgical weight reduction interventions induce an average of ~10%–15% initial weight reduction from initial body weight [27], often with only ~50% of the weight reduction maintained after one year [28,

Table 4
Estimated degree of mean weight reduction and clinically meaningful improvement in health outcomes [26].

Degree of weight reduction associated with improvement in health condition	Medical conditions
≥2.5% weight reduction	Improvement in glucose metabolism Reduction in triglyceride blood levels Improvement in polycystic ovary syndrome and infertility
≥5.0% weight reduction	Improvement in Impact on Weight on Quality-of-Life score Improvement in depression Improvement in mobility Improvement in knee functionality, as well as improvement in walking speed, distance, and pain among patients with knee osteoarthritis Reduction in hepatic steatosis Improvement in urinary incontinence Improvement in sexual function Increase in high density lipoprotein cholesterol levels Improvement in health care costs
≥10% weight reduction	Improvement in sleep apnea Improvement in non-alcoholic steatohepatitis
≥16% weight reduction	Potential reduction in cardiovascular and overall mortality

Table copied with permission from Ref. [27].

29]. Successful weight reduction maintenance usually requires a similar combination of interventions required for initial weight reduction [28]:

- Appropriate nutrition [10].
- Routine physical activity [10].
- Behavior training [11].
- When appropriate, initiation or continuation of pharmacologic anti-obesity therapy and/or consideration of bariatric surgery [9,27].

Factors that favor weight regain include physiologic priority imbalances, neurobiological reactions to weight reduction, decreased resting metabolic rate, greater musculoskeletal efficiency, and behavior reversion [2,28–30]. "Metabolic adaptation" or "adaptive thermogenesis" refers to the reduction in resting metabolic rate with weight reduction, beyond that predicted from the loss of body weight and the corresponding changes in fat and lean tissues [31]. This effect may be mainly during periods of active negative energy balance, with post weight reduction resting metabolic rate potentially most dependent on the patient's energy balance [32].

Whether it be the experience of clinical trials, or the experience of clinical practice, weight reduction among patients with obesity is frequently successful. What is less successful is weight reduction maintenance [33]. In patients with obesity, increased energy expenditure through physical activity is among the more validated determinants of weight reduction maintenance [28]. But whether it be healthful nutrition or routine physical activity, the success of weight reduction maintenance is enhanced with [34]:

- Continuous monitoring
- Goal setting
- Sustained motivation
- Facilitating and acknowledging successes and positive experiences to counterbalance the frequent challenging, frustrating, and potentially negative experiences that often accompany efforts to attain and maintain a healthy body weight

3.1.5. ***MMO #5:*** *In patients with obesity, increased body fat is the cause of all their health conditions*

Patients with obesity often do not receive standard preventive medical care due to challenges in healthcare access, as well as discriminatory bias and stigma [3,35]. Complicating medical care of the patient with obesity is the common scenario wherein signs and symptoms unrelated to obesity are often dismissed as being due to obesity, without further consideration or evaluation. It is true type 2 diabetes mellitus is commonly caused by the adiposopathic consequences of obesity. However, type 2 diabetes mellitus can also be caused by more rare conditions such as hemochromatosis, hypercortisolism, excessive growth hormone, pancreatic insufficiency, side effects of concomitant therapies, genetic syndromes of insulin resistance, and genetic syndromes of limited pancreatic insulin secretion [36]. High blood pressure is commonly caused by the adiposopathic consequences of obesity. However, high blood pressure can also be caused by more rare conditions such as pheochromocytoma, primary hyperaldosteronism, hypercortisolism, hyperthyroidism, renal artery stenosis, kidney diseases, side effects of concomitant therapies, and familial or genetic syndromes [37]. Dyslipidemia is commonly caused by the adiposopathic consequences of obesity. However, dyslipidemia can also be caused by untreated hypothyroidism, poorly controlled type 2 diabetes mellitus, liver disease, kidney disease, side effects of concomitant therapies, and genetic dyslipidemias [38]. While the adiposopathic consequences of obesity may commonly contribute to many other chronic diseases such as sleep apnea, osteoarthritis, cancer, cardiovascular disease, and depression, each of these diseases have other potential causes or contributors beyond obesity alone. In summary, while obesity can and does contribute to a myriad of adverse health consequences, obesity as the etiology of a patient's presentational signs and symptoms is best considered part of a differential diagnosis, and not assumed to be the singular cause for every problem encountered by the patient.

3.1.6. ***MMO #6:*** *people are predestined towards obesity due to an unalterable "setpoint"*

Positive caloric balance may lead to adipocyte hypertrophy with variable increases in adipocyte proliferation [39]. Individuals are not born with a fixed number of fat cells. Adipocytes undergo ~10% turnover per year, and individuals without obesity may have 25–35 billion fat cells, while individuals with obesity may have 100–150 billion fat cells [39].

In an otherwise healthy person at a given body weight, weight stability is defended by physiologic mechanisms. The body strongly defends against weight reduction and weakly defends against weight gain. This is somewhat analogous to the body's reaction to high and low blood sugar. High blood sugar is often relatively asymptomatic. Conversely, low blood sugar typically elicits a profound response that prompts urgent caloric intake (e.g., hunger and adrenergic responses such as tachycardia, sweating, and confusion). While the forces that prompt body weight regain do not include increased adrenergic responses, this example highlights that the body has disproportionate responses to increased and decreased blood sugar. Similarly, the body has disproportionate responses to increased and decreased body weight. During initial weight reduction due to negative caloric balance, energy expenditure decreases (e.g., reduced resting metabolic rate and reduced physical activity energy expenditure), blunting the expected weight reduction if calculated solely on the number of reduced calories ingested [40]. Additionally, hunger hormones increase and satiety hormones decrease, promoting weight regain. One of the lyrics in Joni Mitchell's 1970 song, "Big Yellow Taxi" is *you don't know what you got 'till it's gone.* This "Big Yellow Taxi effect" is one way to conceptualize why weight regain is so common after weight reduction. Prior to weight reduction in a patient with increased adiposity, the increase in satiety/anti-hunger hormones may have not been sufficient to prevent obesity. However, once satiety/anti-hunger hormone levels diminish with weight reduction, then the effects of these satiety/anti-hunger diminish as well. The loss of satiety/anti-hunger hormones effects during weight reduction in patients with obesity, coupled with increased hunger hormones and decreased in resting metabolic rate, helps favor weight regain.

If the body weight "setpoint" is defined as the average of a person's generally narrow range of body weight at a point in a person's life, then this range is determined by age, height, sex, genetics, neurologic function, nutritional intake, physical activity, behavior, environmental factors, physical and mental health, and satiety/hunger hormones [33,40,41]. Figs. 1–3 show factors that influence bodyweight setpoint, hormone adaptations, and ways to alter a "setpoint."

With weight reduction due to negative caloric balance, body mass is decreased, usually with a reduction in both fat and muscle mass, although that can be variable depending on the degree of physical activity/exercise during weight reduction. Resting metabolic rate decreases and hunger hormones increase. When weight reduction stabilizes, then this establishes a new "setpoint", with alterations in factors noted in Fig. 1.

3.1.7. ***MMO #7:*** *most people with increased body fat are generally healthy and will remain healthy*

Obesity is a disease of excess adipose tissue with anatomic and/or functional abnormalities that manifest as illness, sickness, or ailment (See Table 2.). Obesity is a disease that increases morbidity and mortality [42–47]. Obesity promotes "fat mass" disease (e.g., orthopedic abnormalities potentially leading to immobility, sleep apnea, skin friction) [3,48]. Obesity promotes "sick fat" disease or adiposopathy, which frequently contributes to the most common metabolic conditions encountered in clinical practice such as type 2 diabetes mellitus, hypertension, dyslipidemia, and thrombosis), which are major cardiovascular disease (CVD) risk factors, and which indirectly contributes to CVD [4,

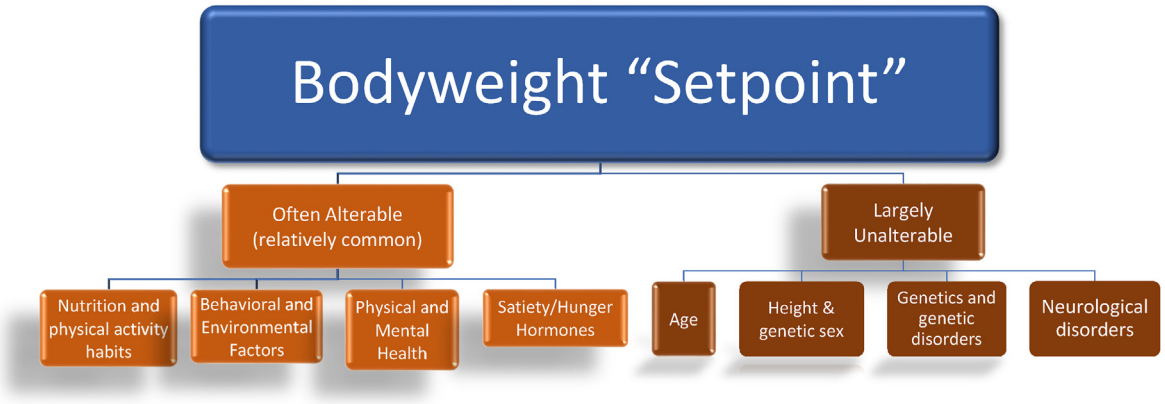

Fig. 1. Bodyweight "Setpoint." Some patients with obesity are said to be "set in their ways," with established habits, behaviors, and environmental factors (e.g., social/familial culture) contributing to a bodyweight setpoint. Physical and metabolic health (e.g., mobility, insulin sensitivity/resistance) and various hormones can also contribute to bodyweight setpoint. Weight reduction maintenance may be achieved by establishing a new setpoint via altering these factors. Gravitation back towards prior habits, behaviors, environmental factors, and ill-health may result in weight regain and return to a setpoint closer to before weight reduction. The effects of weight reduction on satiety/hunger hormones are variable, with a potential long-term (1 - 2 years) hormonal changes that may favor weight regain compared to before weight reduction. Body weight reduction reduces resting metabolic rate, which contributes to a multifactorial "new setpoint" compared to before weight reduction. The net result of weight reduction is often a new setpoint with increased hunger, reduced metabolic rate, and increased potential for weight regain [33,40,41].

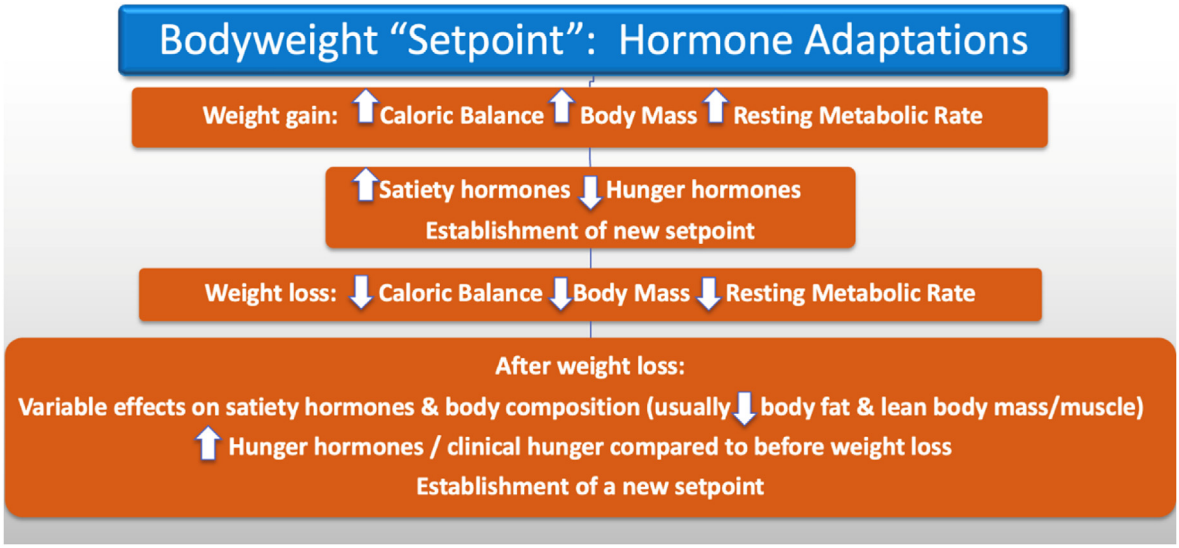

Fig. 2. Bodyweight "Setpoint": Hormone Adaptations. Hormones impact body weight and alter a person's "setpoint," often by impacting satiety and hunger [33,40,41]. An increase in body weight is generally due to an increase in caloric balance, with increased fat and muscle mass and increase in resting metabolic rate. While often ineffectual in preventing an increase in body fat, satiety hormones are typically increased, and hunger hormones are typically decreased. Once all these factors are stabilized, then this helps to establish a new "setpoint."

48]. Obesity may directly contribute to CVD via adiposopathic epicardial effects [42,44,49,50]. Obesity also increases the risk of cancer [5].

Some individuals are reported to have metabolic healthy obesity (MHO). However, no universally accepted definition exists for MHO. Given the variation in definitions, more detailed evaluations for metabolic disease due to obesity are associated with lower reports of the prevalence of MHO [51–53]. Thus, the prevalence of MHO substantially depends on the diagnostic criteria (i.e., rates ranging from 6 to 75%) [51,53]. Patients with MHO also have higher rates of heart disease and heart failure [49,54]. Patients with MHO also experience fat mass diseases such as sleep apnea, stress/damage to joints, and increased risk of cancers [4,48]. With aging, 30–40% of patients with MHO develop metabolic disease within 6 years [55].

Type 2 diabetes mellitus is diagnosed by high blood sugar. Especially at early onset, high blood sugar may not manifest signs or symptoms. Nonetheless, few would argue that because some patients have minimal to no signs or symptoms, type 2 diabetes mellitus is not a disease. Hypertension is diagnosed by high blood pressure. Especially at early onset, high blood pressure may not manifest signs or symptoms. Nonetheless, few would argue that because some patients have minimal to no signs or symptoms, hypertension is not a disease. Hypercholesterolemia is diagnosed by high blood cholesterol. Especially at early onset, high cholesterol may not manifest signs or symptoms. Nonetheless, few would argue that because some patients have minimal to no signs or symptoms, hypercholesterolemia is not a disease. Obesity is diagnosed by increased body fat. While some patients with obesity may not currently manifest severe signs or symptoms, this does negate that obesity fulfills accepted definitions as a disease (See Section 3.1.1 and Table 2).

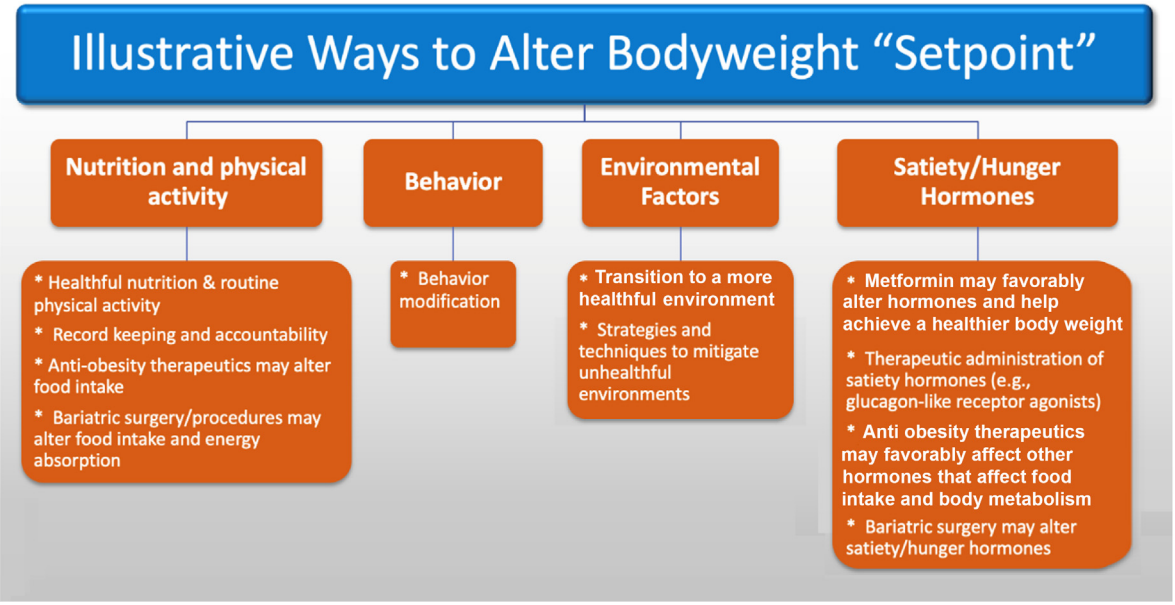

Fig. 3. Illustrative Ways to Alter Bodyweight "Setpoint."The body's "setpoint" is not fixed and may be altered through factors such as nutrition, physical activity, behavior, environmental factors, and hormones [33,40,41].

3.2. *Etiology*

3.2.1. ***MMO #8:*** *obesity is mostly due to a defined genetic abnormality*

Many patients believe their obesity is primarily due to their "genes." However, obesity is not usually due to a defined genetic abnormality, such as a recognized obesity syndrome and/or identifiable monogenetic mutation of a single gene. Furthermore, it is unlikely that the dramatic rise in the prevalence of obesity over the past decades to centuries is due to a world-wide introduction of a universal gene mutation. More likely is that obesity is mostly due to changes in population ecosystems [56]. That said, obesity does have genetic and familial components (See Fig. 4.) Some estimates suggest that 60% of obesity influenced by inheritance is due to polygenetic, non-Mendelian transmission of two or more genes.

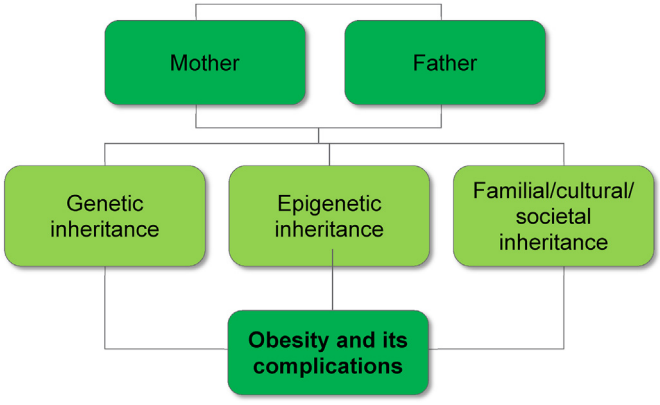

Fig. 4. Genetic, epigenetic, and familial/cultural/societal factors potentially contribute to obesity [7]. For the purposes of this figure, "Mother" is intended to identify the female origin of the egg. "Father" is intended to identify the male origin of the sperm. The terms Mother and Father are also intended to metaphorically represent caregivers of offspring – which may not necessarily by the patient's biologic Mother or Father. Epigenetic modifications involve alterations in genetic expression (e.g., deoxynucleic acid methylation and demethylation and histone modification), and not alterations in the gene sequencing. Alterations in epigenetic gene expression influences the predisposition of individuals to common metabolic diseases such as obesity, diabetes, cardiovascular disease and cancer [5,57,58].

Beyond inheritance of genetic sex (which affects body composition), polygenetic inheritance accounts for common expressed traits that affect hunger/appetite, as well as traits that affect resting metabolic rate and energy expenditure such as height, muscle mass, and energy efficiencies regarding energy (i.e., fat) storage and heat generation [8,57] (See Fig. 5).

Polygenic obesity can be due to genetic variants that alone, may have only a modest effect on the phenotype. Gene variants (alleles) that have small influences on body weight are termed polygenes [59]. However, when combined with other predisposing variants, the collection of gene variants can result in clinically meaningful phenotypic expressions. Historically, using genome-wide association studies (GWAS), the fat mass and obesity associated (FTO) gene was discovered in 2007, and found to be involved in posttranslational modification, deoxynucleic acid repair, and fatty acid metabolism. The FTO gene was the first gene associated with an increase in body mass index [60]. The FTO gene (located on chromosome 16) and its polygenic variants are widely expressed in multiple body tissues, including the brain. Among obesity-related genes, the FTO gene has one of the strongest links with obesity in the human population [61]. GWAS analyses have identified multiple single nucleotide polymorphisms (SNPs) of the FTO genes, which increase the risk for obesity and metabolic syndrome [62].

Tables 5 and 6 list some genetic abnormalities associated with obesity. Syndromic obesity is a term that reflects patients having a distinct set of clinical phenotypes (e.g., dysmorphic features, variances in height, intellectual impairments), attributable to abnormalities in sections of chromosomes, and often named after the person/s who described the syndrome. Monogenic obesity is mostly due to autosomal recessive abnormalities of a single gene of the leptin-melanocortin pathway, such as the mutation of the leptin gene on chromosome 7, leptin receptor gene on chromosome 1, proprotein convertase subtilisin/kexin 1 (PCSK 1) gene located on chromosome 5, or proproopiomelanocortin (POMC) gene located on chromosome 2) [57].

Finally, while the genetic makeup of the individual cannot be altered, the hormonal profile of an individual can be altered, independent of genetic makeup. For example, transgender individuals (i.e., individuals whose gender does not align with sex assigned at birth) may receive gender affirming hormone therapy (e.g., estrogens, anti-androgens, testosterone, or gonadotropic releasing hormone therapy) or gender affirming surgery (e.g., gonadectomy and other surgeries) [63]. Beyond

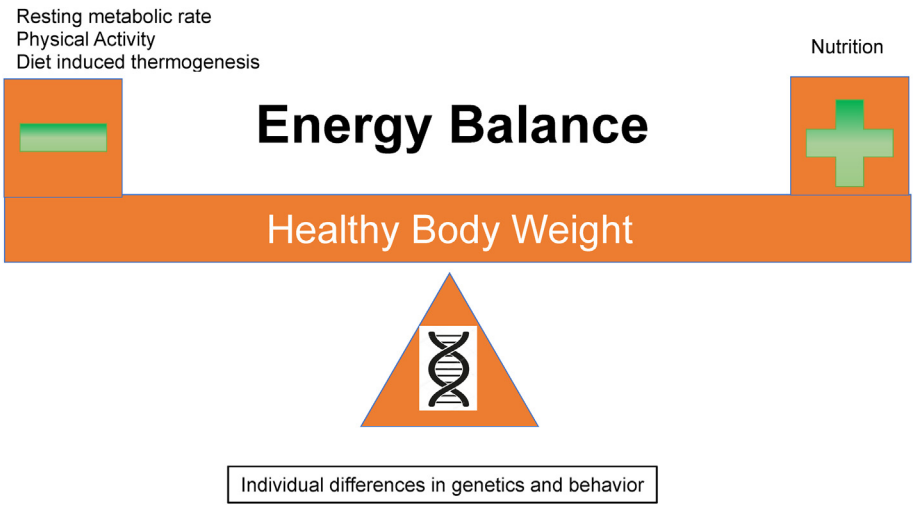

Fig. 5. Body Weight Homeostasis. Variance exists among individuals regarding resting metabolic rate (RMR). RMR is increased among younger individuals and genetic factors such as male sex, increased height, and increased muscle. Obesity may also increase RMR, largely due to increased energy required to maintain the increased body tissues (i.e., increased adipose tissue and if applicable, increased muscle mass). Beyond RMR, other common contributors to variances in energy expenditure include non-exercise activity thermogenesis (NEAT), physical activity, and diet-induced thermogenesis (DIT). Finally, RMR can be affected by climate. Hotter environments increase RMR to cool the body; colder environments increase RMR through non-shivering thermogenesis to warm the body [8].

health care disparities related to obesity alone, transfeminine individuals (i.e., those assigned male at birth who identify as a woman) and transmasculine individuals (i.e., those assigned female at birth who identify as a man) may also encounter health care disparities based upon their sexual identification/orientation [64]. Additionally, transgender individuals may also have an increase in body weight after initiation of gender affirming hormone therapy, potentially prompting the consideration of multidisciplinary weight-reduction interventions [65]. Androgen administration may increase muscle mass (i.e., potentially increasing body weight while limiting an increase in percent body fat) and estrogen administration may facilitate preferential fat deposition in the gluteal-femoral depots [66] The effect of gender affirming hormone therapy and gonadal surgery on resting metabolic rate and body composition await the results of clinical trials [67]. Similarly, current data is insufficient to definitively assign the risk of gender affirming hormone therapy regarding coronary artery disease, stroke, hypertension, thrombosis, lipid abnormalities, and diabetes mellitus. Some existing epidemiological data suggests that estrogen administered to transfeminine individuals has the potential to increase the risk of myocardial infarction and ischemic stroke. Conversely, administration of testosterone to transmasculine individuals has inconsistent data regarding increased risk of cardiovascular or cerebrovascular disease [68], although some data suggests that long term testosterone administration to transmasculine individuals without obesity may increase visceral fat [69].

3.2.2. ***MMO #9:*** *In the absence of a genetic or secondary medical cause, obesity is mostly due to a lack of willpower*

Obesity is often the result of an imbalance in physiologic forces affecting hunger that strongly resist weight reduction and weakly resist weight gain [2]. Beyond the genetics, biology, and secondary causes, behavioral factors that can predispose to obesity include emotions, habit time cues, environment, information gap, and reward factors [11]. Emotional stress can contribute to obesity due to impairment of self-regulation and may promote the choice of more unhealthful (immediately rewarding ultra-processed) foods over more healthful (delayed-gratification unprocessed) foods [11]. Eating disorders, such as binge-eating disorder, bulimia nervosa, and night-eating syndrome, can also affect eating behavior [11,70–72]. Physical inactivity behavior may be due to ill health (e.g., musculoskeletal, neurologic, pulmonary, cardiac, and other health disorders), disinterest, lack of prioritization, lack of safe availability to physical activity environment, or utilization of conveniences [2,11]. Thus, many factors contribute to nutrition and physical activity behaviors, well beyond "willpower."

Many highly motivated individuals with extraordinary willpower are successful in other aspects of their lives, largely due to their skill, work ethic, and their prioritization towards maximizing efficiencies. While acknowledging exceptions exist, an illustrative subset of successful individuals that might be considered "motivated" or having "willpower" would include college students or college-educated adults. During college, a 2011 analysis concluded that students generally gained weight, with overweight/obesity increasing from 23% to 41% during their college experience [73]. After college, one report estimates that over 30% of excess total deaths were attributable to central obesity among college-educated adults (compared to 1–10% among less-educated counterparts) and 60–70% of excess cardiovascular deaths [74].

Given the health importance of obesity and given the degree of effort required for success in higher education, it would be challenging to argue that the increase in body weight among those attending and graduating from college is solely due to a lack motivation or willpower. An alternative explanation is that the same advantages afforded by an efficiency mindset regarding many life successes may be disadvantageous regarding healthful nutrition and physical activity. This helps explain why many otherwise successful individuals find their obesity uniquely challenging. Breaking the efficiency mindset via implementing nutritional, physical, and behavioral inefficiencies may translate into less efficient ability to store body fat, and thus help achieve a healthier body weight.

For example, in contrast to more convenient (and thus more efficient) ultra-processed food intake, consuming unprocessed food may promote greater inefficiency in gastrointestinal energy absorption and post-absorptive conversion to fat. Compared to many ultra-processed carbohydrates, dietary intake of unprocessed whole food fruits and vegetables, and high fiber complex carbohydrates generate less post-prandial insulin secretion, resulting in less efficient storage of energy in fat stores [10]. Alterations in the microbiota may result in less efficient gastrointestinal energy absorption [75]. Growth of muscle mass may increase energy demand independent of physical activity and increase non-shivering thermogenesis [76]. Increasing muscle mass via resistance training may reduce skeletal muscle work efficiency [77]. Conversely, training the same muscles may reduce the energy cost of physical exercise through adaptive biomechanical efficiency. Thus, varying the type of exercise is sometimes recommended to increase or maintain energy expenditure by avoiding biomechanical efficiency [78]. Less efficient physical exercise techniques can increase energy expenditure (e.g., not holding treadmill handles). Less efficient non-exercise activity thermogenesis (NEAT) can increase energy expenditure (e.g., walking instead of more efficient automated travel; stairs instead of elevators, choosing a less efficient parking space further from the destination) [79]. Less

Table 5
Examples of genetic abnormalities and obesity.

Clinical abnormality	Illustrative Clinical Presentations[a]	Genetic Abnormality
Achondroplasia	• Obesity • Short stature • Not usually associated with intellectual impairment • Macrocephaly • Prominent short arms and legs • Prominent abdomen • Short hands and fingers • Low muscle tone in infancy	• Mutation of fibroblast growth factor receptor 3 gene (FGFR3)
Alstrom Syndrome	• Obesity • Short stature • Intellectual impairment not a consistent feature, although loss of sight and hearing complications may make learning more difficult • Photophobia • Nystagmus • Blindness (cone rod dystrophy) • Deafness • Insulin resistance, type 2 diabetes, acanthosis nigricans • Hypertriglyceridemia • Cardiomyopathy • Kidney, lung, and liver dysfunction	• Mutation of Alstrom Syndrome Protein-1 (ALMS1) gene
Albright's Hereditary Osteodystrophy	• Obesity • Short stature • Intellectual impairment • Rounded face • Skeletal defects: shortened fourth metacarpals and other bones of the hands and feet • Dental hypoplasia • Soft-tissue calcifications/ossifications • Pseudohypoparathyroidism (hypocalcemia, hyperphosphatemia)	• Associated with molecular defect in the guanine nucleotide binding protein alpha stimulating gene (GNAS1) described as located on chromosome 20, which encodes for the alpha subunit of the stimulatory G protein
Bardet–Biedl Syndrome	• Obesity • Short stature • Intellectual impairment • Metabolic abnormalities (e.g., type 2 diabetes mellitus, high blood pressure, dyslipidemia) • Blindness/retinitis pigmentosa (retinal dystrophy and pigmentary retinopathy) • Hearing loss and anosmia • Cardiomyopathy and aortic stenosis • Dysmorphic extremities: polydactyly and short or fused fingers and toes • Poor coordination • Dental abnormalities • Behavioral/emotional challenges • Male hypogonadism (with infertility) • Femail genital and urinary tract abnormalities • Renal cystic disease and renal insufficiency, which may lead to end-stage renal disease • Premature aortic stenosis	• Autosomal recessive • Mutations of at least 20 genes (BBS genes) applicable to cilia involved in: o Cell movement o Chemical signaling o Sensory input (sight, hearing, and smell)
Beckwith-Wiedemann Syndrome	• Obesity • Unless due to hypoglycemia, usually not associated with intellectual impairment • Macrosomia • Macroglossia • Hepatosplenomegaly • Hypoglycemia • Tumors	• Mutation of gene on chromosome 11 (11p15.5) • Sometimes considered the most common overgrowth and cancer predisposition disorder
Borjeson-Forssman-Lehmann Syndrome	• Obesity • Short stature • Intellectual impairment • Seizure disorders • Hypogonadism males and females • Gynecomastia • Large earlobes • Tapered fingers and shortened toes	• X-linked recessive disorder • Most often fully expressed in males • Girls are usually not affected or only mildly affected; however, they may be carriers • Mutation of the zinc plant homeodomain-like finger gene PHF6, located on the X chromosome
Carpenter Syndrome	• Obesity • Short stature • Intellectual impairment • Premature closure of the fibrous joints (cranial sutures) between bones of the skull (craniosynostosis) • Top of the head appears pointed (acrocephaly) • Webbing or fusion (syndactyly) of fingers or toes (digits) • Short fingers and toes (brachydactyly) • Extra digits (polydactyly)	• In most instances, caused mutations in the Ras-associated binding proten 23 (RAB23) gene • Acrocephalopolysyndactyly disorder

(*continued on next page*)

Table 5 (*continued*)

Clinical abnormality	Illustrative Clinical Presentations[a]	Genetic Abnormality
Cohen Syndrome	• Obesity • Short stature • Intellectual impairment • Hypotonia • Developmental delay • Small head size (microcephaly) • Narrow hands and feet • Chorioretinal dystrophy • Joint hypermobility • Thick hair, eyebrows, and eyelashes • "Open mouth" expression with incisor prominence and high narrow roof of mouth • Low white blood cell count (neutropenia) • Friendly behavior	• Typically autosomal recessive • Mutation of the vacuolar protein sorting 13 homolog B (VPS13B) gene, also known as the COH1 gene in chromosome 8 (8q22)
Down Syndrome	• Obesity • Short stature • Intellectual impairment • Hypotonia • Smaller head • Short neck • Small ears • Single palmar crease	• Trisomy 21 (three copies of chromosome 21)
Fragile X Syndrome	• Obesity • Short stature • Intellectual impairment • Large forehead • Long face • Prominent forehead and jaw • Protruding ears • Macro-orchidism (enlarged testicles)	• Mutation of Fragile X Messenger Ribonucleoprotein 1 (FMR1) gene
Melanocortin 4 Receptor Deficiency	• Obesity, especially in families • Hyperphagia and obesity early in childhood • Insulin resistance • Increase in bone mineral density ("big boned") • Accelerated linear growth • Reduced sympathetic nervous activity with potential relative decreases in blood pressure, heart rate, and urinary catecholamine excretion	• Autosomal dominant, recessive, or codominant • Most known inherited monogenetic defect predisposing to obesity • Polymorphism of melanocortin 4 receptor (MC4R) gene localized to chromosome 18
Prader–Willi Syndrome	• Obesity, often hyperphagic • Short stature • Insatiable appetite • Intellectual impairment • Weak muscle tone (hypotonia) • Poor growth • Small hands/feet • Delayed development • Underdeveloped genitals (often with infertility) • Behavioral/emotional challenges • Narrow forehead • Almond-shaped eyes • Triangular mouth • Often with fair skin and light-colored hair	• Not an inherited disease; caused by random genetic error • Most cases involve loss of function of a portion of chromosome 15 (e.g., 15q11-13) • Often reported as the most common human genetic "obesity syndrome"
Turner Syndrome	• Obesity • Short stature • May have intellectual impairment • Premature ovary failure with infertility • May have failure to attain puberty • Congenital heart disease • Short and webbed neck • Low hairline at the back of the head and low-set ears • Retrognathia, strabismus, amblyopia, high arched roof of mouth • Narrow fingernails and toenails turned upward • Broad chest with widely spaced nipples ("shield chest")	• Absence or dysfunction of an X chromosome • Affects females

Shown are examples and descriptions of genetic abnormalities associated with obesity [57]. https://rarediseases.org/(National Organization for Rare Disorders).

[a] Not all patients will have all these clinical findings.

efficient in-person store-shopping (i.e., increased walking) for food and merchandise may expend more energy than online shopping and home delivery. Less efficient periodic breaks from sedentary work may increase daily steps and increase energy expenditure [2]. In short, over the past decades, including the past 10 years, body weight has increased [80], with little to no evidence that this weight gain is due to a loss of global will. Many individuals with obesity have extraordinary willpower towards achieving school, work, and life efficiency, which has largely contributed to their successes. For many patients, embracing a "be inefficient" mindset regarding obesity management may help facilitate attainment of a healthier body weight.

3.2.3. ***MMO #10:*** *obesity is solely due to eating too much*

While commonly suggested as a universal "cure" for obesity, the "Eat Less & Move More" mantra has not proven effective in reversing the global obesity epidemic [81]. Energy expenditure myths ("Move More")

Table 6
Additional genetic abnormalities associated with obesity [1].

Examples of Genetic Abnormalities Leading to Obesity and Short Stature[a]	Examples of Genetic Abnormalities Leading to Obesity, Dysmorphic Features, and Intellectual Impairment[a]
Achondroplasia	Albrights Hereditary Osteodystrophy
Albright's Hereditary Osteodystrophy	Bardet-Biedl Syndrome
Alstrom Syndrome	Borjeson-Forssman-Lehmann Syndrome
Bardet-Biedl Syndrome	Carpenter Syndrome
Borjeson-Forssman-Lehmann Syndrome	Cohen syndrome
Carpenter Syndrome	Downs Syndrome
Cohen Syndrome	Fragile X Syndrome
Down Syndrome	Prader-Willi syndrome
Fragile X Syndrome	Turner syndrome
Prader-Willi Syndrome	
Turner Syndrome	
Other genetic abnormalities or syndromes[a]	
Deletions/mutations of various gene loci 17 and polymorphisms of fat mass and obesity associated (FTO) gene located on chromosome 16	Prohormone convertase-1 deficiency
Brain derived neurotrophic factor (BDNF) deficiency	Proopiomelanocortin deficiency
Carboxypeptidase E mutations	Proprotein convertase subtilisin kexin 1/3 deficiency
Hypoventilation and Autonomic Dysregulation (ROHHAD syndrome)	Rapid-onset Obesity with Hypothalamic dysfunction
Leptin deficiency (due to gene mutation)	Rubinstein-Taybi syndrome
Leptin receptor deficiency	Sim1 deficiency
Macrosomia, Obesity Macrocephaly Ocular abnormalities (MOMO) syndrome	Src homology 2 B adapter protein 1 (SH2B1) mutations
Maternal uniparental disomy of chromosome 14	TrkB deficiency

Shown are genetic abnormalities associated with obesity and short stature, obesity and dysmorphism and intellectual impairment, and a list of other genetic abnormalities, not previously listed in Table 5.

[a] These are not exhaustive lists; not all patients will have these signs/symptoms.

are addressed later in this Clinical Practice Statement. Regarding "Eat Less," this phrase seems to suggest that caloric intake is solely dependent on the amount of food consumed. However, the energy stored as body fat is a net balance between macronutrient energy absorbed from the gastrointestinal tract (not necessarily amount of food consumed) less energy expended [82]. The obesogenic effect of macronutrients is dependent on the quantity, quality, and caloric density of food, not exclusively the gram quantity of food (See Fig. 6.).

Macronutrients differ in their stored energy potential. Carbohydrates serve as a source of energy at approximately 4 kcal/gram, fats at 9 kcal/gram, proteins at 4 kcal/gram, and alcohol at 7 kcal/gram [10]. Thus, for the same "amount" of dietary intake, foods with more fat (and alcohol) are more energy dense and will have more calories per amount (gram) than foods less energy dense. If fiber is removed via ultra-processing, then concentrated sugars can also have high energy density (i.e., candy, sugared juices/drinks). Combination fat and sugar foods with high energy density can include fried snacks, cookies, pies, and cakes [83]. The adverse impact of energy dense foods on caloric intake and obesity is a rationale why the Obesity Medicine Association recommends that patients with obesity: "Avoid energy dense foods and beverages" [10].

The amount of food consumed is the sum of digestible and indigestible foodstuffs. Polysaccharides (chain of simple sugars) include glycogen (i.e., branched polysaccharide of glucose found in animals), starch (i.e., branched and chain polysaccharide of glucose found in plants), chitin (i.e., structural carbohydrates for exoskeleton of arthropods and cell walls of fungi), and plant cell wall structural elements such as cellulose, hemicellulose, and pectin. Lignin is a non-carbohydrate phenolic aromatic polymer that makes up cell wall thickenings of cells in the plant vascular tissue [84]. Termites and ruminants (i.e., cattle) have bacteria in their rumens that release cellulase that help breakdown cellulose (lignin is not effectively digested in most ruminants) for intestinal nutrient absorption [85,86]. However, humans do not have rumens, and do not have the necessary enzymes or intestinal micro-organisms to effectively digest cellulose, hemicellulose, pectin and/or lignin.

Thus, especially regarding consumption of plant-based foods, a substantial "amount" of the dietary intake of foodstuffs does not result in intestinal energy absorption. Whole fruits and vegetables are often ≥90% water by weight. Additionally, plant-based foods have indigestible water insoluble fiber (e.g., cellulose, hemicellulose, and lignin) and water soluble fiber (e.g., pectin, gums, and mucilages) [87].

Regarding fibrous plant foods, non-starchy leafy greens, such as cabbage, brussels sprouts, and lettuce and other salad greens, along with zucchini, peppers, asparagus, and tomatoes often provide more grams of fiber per 100 grams of dry weight than starchy white potatoes, sweet potatoes, yams, corn, beans, carrots, beets, turnips, and winter squashes. That said, regarding nutrition quality, starchy vegetables/fruits remain closer to non-starchy vegetables and fruits, than to candy and soda [88]. In general, increased plant-based fiber allows for an increase in the gram "amount" of food consumed, with most of the volume and weight consisting of contents not digested for energy storage (e.g., water and fiber) [87].

Some evidence suggests that high fiber intake may increase fullness with meals and contribute to modest weight reduction [12]. Medicinally,

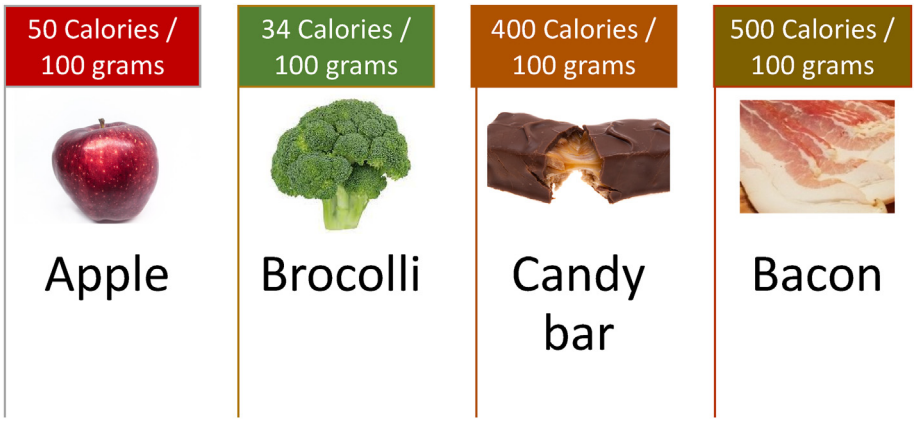

Fig. 6. Energy density of foods. The caloric intake of foods is not only dependent on the amount of food, but also the caloric density of food. Shown examples of the variance in kcal or Calories of foods per 100 grams of each food.

a biodegradable oral non-systemic superabsorbent hydrogel, made from cross-linked carboxymethylcellulose and citric acid, promotes fullness and may increase satiety and is indicated to aid in wight management in adult patients with overweight or obesity [27]. In short, depending on food content, variance exists in the amount of food consumed by humans, the energy content of food, and the degree food can be digested. When added to the micronutrient benefits of plant-based foods (i.e., which may reduce the risk of cancer and cardiovascular disease) [5], this all helps explain the rationale why the Obesity Medicine Association recommends patients with obesity be encouraged to prioritize: "vegetables, leafy greens, fruits, berries, nuts, seeds, legumes, and whole grains" and "high-fiber foods over low-fiber foods" [10].

3.2.4. ***MMO #11:*** *obesity is unrelated to the caloric content of food*

Some clinicians (and some authors) believe that "calories in equals calories out" is scientifically disproven, with the suggestion that obesity energetics are exempt from the Laws of Thermodynamics [89]. The First Law of Thermodynamics states that while energy can be transformed, it can neither be created nor destroyed [90]. This First Law of Thermodynamics is sometimes characterized as mainly a "bookkeeping" law [91], reflecting the unalterable balancing of energy and matter. As such, it is a basic law of physics that "calories in" does indeed equals "calories out" [82]. To deny that caloric consumption is relevant to obesity is to deny the rationale and utility of two essential pillars of obesity management (nutrition and behavior). Healthful nutrition and behavior have concurrent and sentinel objectives to encourage patients with obesity to avoid consumption of, and avoid easy access to, energy dense-foods [10,11].

The unalterable truth is that regarding obesity, caloric intake does matter [82].

That said, perhaps a more applicable focus might be the Second Law of Thermodynamics that describes the relationship between energy available to do work, and entropy, which is a measure of how much energy is not available to do work [91]. The Second Law of Thermodynamics acknowledges inefficiencies in energetic systems such that not all heat energy can be converted into work and that non-equilibrium work-energy potential is dissipated as heat [92] In living beings, not all food energy is utilized to perform work. Consistent with the second law of thermodynamics, inefficiencies exist in biological systems. The more efficient the muscle movement, enzymatic reactions, or membrane transport, then the less heat is generated. The less efficient the biologic system, then the more heat is generated. When viewed from this perspective, the question is not whether "calories in equals calories out," but rather, what is meant by "calories in," what is meant by "calories out" and what are the applicable biologic efficiencies and inefficiencies (See Section 3.2.2).

In most individuals with moderate physical activity, components of total energy expenditure are approximately [8].

- 70% resting metabolic rate (RMR)
- 20% physical activity [exercise activity thermogenesis (EAT) and non-exercise activity thermogenesis (NEAT)]
- 10% diet-induced thermogenesis (DIT)

Resting metabolic rate is largely determined by age, genetics, sex, body size, body composition, body surface area, and environmental climate (See Fig. 5.). Regarding diet-induced thermogenesis (DIT), nutrient energetics begin with food growth, processing, and choices, followed by food consumption. The thermic effect of food (TEF) is the energy required to digest, absorb, and metabolize the macronutrient for storage. Digestion not only involves intestinal hormones and enzymes, but if total body energy expenditure is measured, also involves the microbiome. Intestinal microbes are not only involved in food digestion, but also energy expenditure, and when measured, are involved in total body energy balance [93,94]. TEF is expressed as the percent of the energy potential by the macronutrient (See Fig. 7).

Fats have the lowest TEF; proteins have the highest TEF. The length of time for increased postprandial energy expenditure due to TEF is 0.5 to over 3 hours after a meal [96]. Beyond food intake alone, increased post-prandial energy expenditure can also be due to concurrent caffeine or alcohol consumption, food allergies, medications taken with meals (e.g., decongestants and bronchodilators), supplements, or cigarette smoking with meals.

Those using wearable technologies often find their heart rate increases after meals. Limited data suggests this is related to the TEF. Instead, eating increases blood flow to splanchnic vessels [97], increases

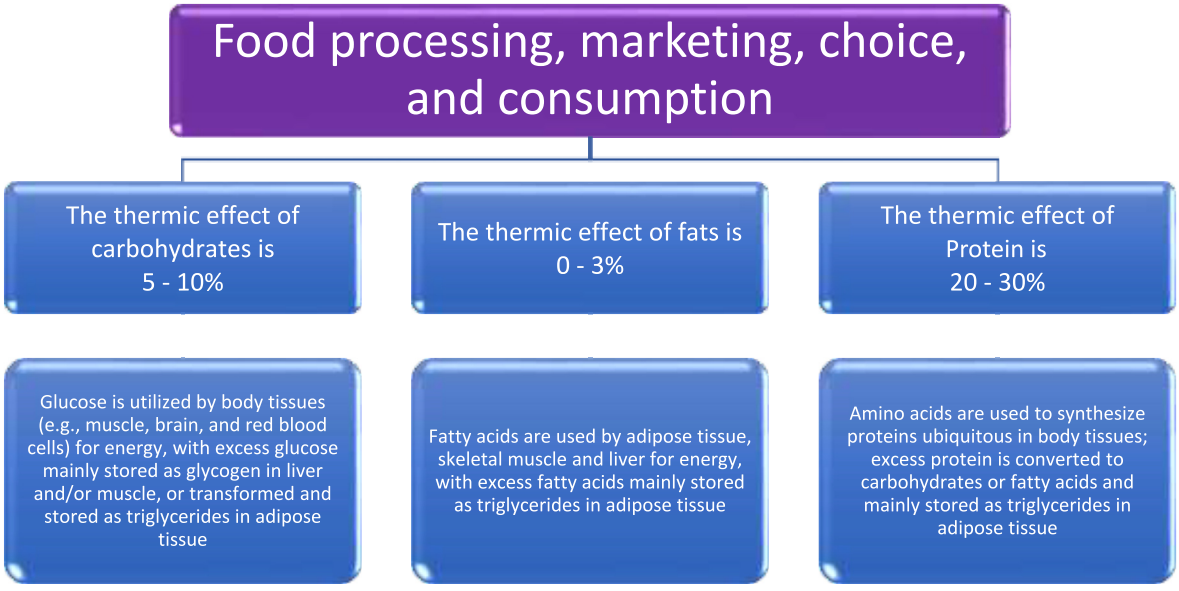

Fig. 7. Food energetics involve food choice, thermic effect of food (i.e., energy required to digest, absorb, and metabolize the macronutrient), and the storage of food macronutrients. After food is processed, marketed, and chosen (all which affect "calories in"), the energetics of food consumption includes: (a) the thermic effect of food reflecting the energy required to digest, absorb, and metabolize the macronutrient, (b) utilization of absorbed and metabolized macronutrients to perform work and other body metabolic processes, (c) and the storage of remaining excess energy – mostly as body fat. The thermic effect of food can be quantified by the percent of the macronutrient energy consumed with its digestion, absorption, and storage metabolism [95].

release of vasoactive peptides, and causes gastric distention such that, when coupled with effects on autonomic nervous and baroreflex systems, can cause relative or absolute reduction in blood pressure (postprandial hypotension) and increased in heart rate. When extreme, postprandial hypotension can be misdiagnosed as "reactive hypoglycemia." The latter can be diagnosed by serial glucose levels taken after mixed meal tolerance test or oral glycose tolerance test [98]. The former can be diagnosed by measuring serial blood pressures (and heart rate) after a meal (as well as tilt table testing if the associated orthostatic hypotension is suspected) [99,100]. From a neurologic standpoint, eating stimulates both the anabolic parasympathetic nervous system [i.e., increases insulin secretion, increases peristalsis, increases gastrointestinal (GI) secretions] and catabolic sympathetic nervous system (promotes thermogenesis, decreases GI motility and secretions, helps maintain postprandial blood pressure through peripheral vasoconstriction to compensate for splanchnic vasodilation). Some patients having bariatric surgery report symptoms of "reactive hypoglycemia." [9] However, low blood sugar and low blood pressure have many of the same signs and symptoms (e.g., tachycardia, sweating, lightheadedness). Some patients diagnosed with "reactive hypoglycemia" may instead have postprandial hypotension. While the incidence is unclear [101], it is sometime reported that orthostatic intolerance may increase after bariatric surgery [102]. However, it is clear that bariatric surgery reduces blood pressure, prompting the reduction of over 30% of antihypertensive medications [103]. Overall, it is the interplay of intestinal neuro-vasal responses to a meal that likely accounts for most of the postprandial increase in heart rate. While it may contribute, little evidence supports the increase in postprandial heart rate is substantially due to the body's reaction to the heat generated from DIT.

Factors that influence TEF include [95,104–111]:

- TEF may be reduced among patients with obesity compared to lean individuals. Some reports suggests that insulin resistance reduces TEF, possibly related to reduced postprandial phase sympathetic nervous system activity. However, the data to support these concepts are inconsistent.
- TEF increases: with: (a) carbohydrate/protein consumption (compared to fat consumption); (b) routine physical activity (i.e., physical exercise), (c) consumption of vegetables, fruits, whole grains, and legumes (as compared to refined grains or animal derived products); (d) consumption of medium chain triglycerides compared to long chain triglycerides; (e) meals consumed earlier in the day; and (f) higher total meal energy intake (irrespective of macronutrient composition)
- TEF may decrease with aging and decrease with consumption of processed versus unprocessed foods
- TEF does not appear to be affected by palatability.
- While consuming a higher energy dense meal may have increased TEF compared to consuming a lower energy dense meal, the TEF consuming an entire daily caloric content in a single meal bolus may not differ to a clinically meaningful degree than the TEF of consuming the same caloric content via multiple meals.
- The effect of meal duration on TEF has varying and sometimes conflicting reports.

The body's generation of heat goes beyond DIT (See Fig. 8). As with the heat generated with food consumption, heat is also a byproduct during the metabolism of stored macronutrients to produce adenosine triphosphate (ATP). Heat is yet again generated when ATP is used to perform work such as muscle movement or drive enzymatic reactions and membrane transport. Management of endogenous and exogenous contributors to body heat is regulated via the hypothalamus [8].

From a body energetics perspective, "respiration" refers to the movement of oxygen and carbon dioxide in and out of cells and is a universal body function not limited to breathing through the lungs. The overall formula describing cellular respiration is [8].

Consumed or Stored Macronutrients (i.e., Food) + Oxygen = CO_2 + H_2O + Energy [~60% Heat & ~40% Adenosine Triphosphate (ATP)]

After eating food, digested glucose from carbohydrates undergoes glycolysis in the cytoplasm of body cells to anaerobically produce 2 three-carbon molecules of pyruvate, ATP, nicotinamide adenine dinucleotide (NADH) and water, with pyruvate being converted to acetyl CoA and entering the citric acid cycle. Digested proteins and fats are also broken down, with their derived acetyl CoA intermediary molecules also undergoing mitochondrial, aerobic enzymatic reactions (e.g., via citric acid cycle, electron transport chain, oxidative phosphorylation). During cellular respiration, when inhaled oxygen from breathing air is combined with the carbon from consumed food, this generates chemical energy, carbon dioxide (CO_2) which is exhaled, and water (H_2O) which is distributed intracellularly, extracellularly, and within the circulation, and potentially excreted (i.e., via urine, breathing, sweating). Regarding the body energetics of chemical energy, both consumed and stored macronutrients are used to create ATP, via enzymatic reactions that also generate heat.

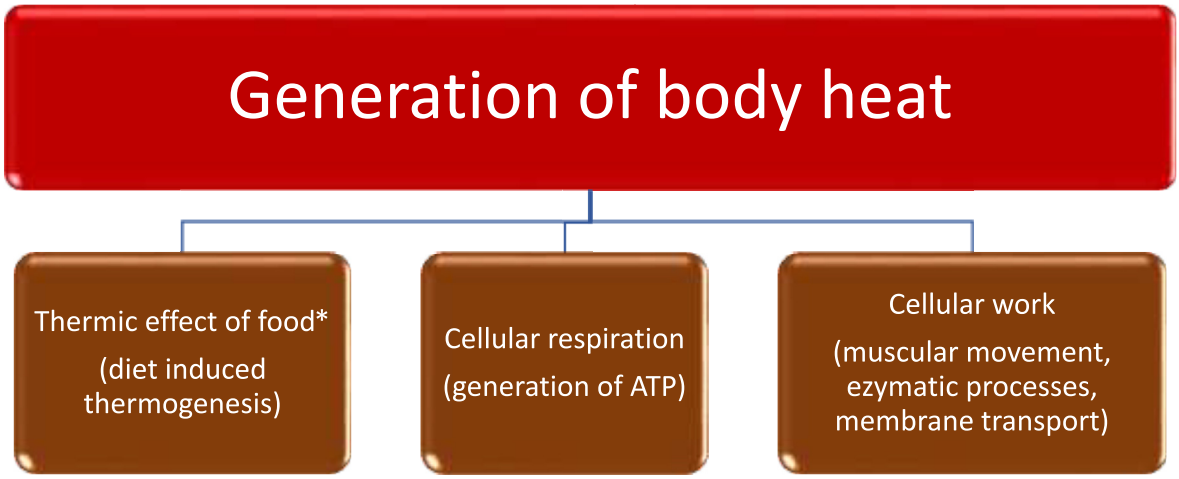

Fig. 8. Body heat origins. Body heat is generated by the digestion and absorption of food, generation of adenosine triphosphate or ATP (i.e., the fuel that drives cellular processes), and when ATP is used to perform cellular work. The heat generated by the cellular work of enzymatic processes can be influenced by hormones (e.g., thyroid hormone), and total body heat is regulated by the brain (i.e., hypothalamus). *Depending on how and when measured, the thermic effect of food may include heat generated by cellular respiration and cellular work.

Once generated, ATP can be viewed like gasoline fuel for motor vehicles. ATP serves to "fuel" functions such as motion (i.e., mechanical work) with the generation of heat (i.e., thermogenesis), at an efficiency of around 30%. Approximately ~70% is released as heat, yet again consistent with the premise that metabolic processes in biologic systems have inefficiency. In summary, intestinally absorbed or stored macronutrients (e.g., carbohydrates, fats, proteins) are utilized to generate ATP, that helps (a) perform work of muscular motion, (b) fuels enzymatic processes, or (c) fuels membrane transport:

- ATP + muscle = muscle contractions + heat
- ATP + biochemicals = metabolic reactions + heat
- ATP + membranes = transport across membranes + heat

The nature of prandial intake of macronutrients and postprandial metabolic processes all influence caloric balance. Regarding "calories in," macronutrients differ in their energy density. The degree ingested foodstuffs are intestinally absorbed depends on the proportion of digestible and indigestible fiber (See Section 3.2.3). Glycemic index/load identifies the degree food content increases postprandial glucose levels. A low glycemic index/load diet is one focused on reducing postprandial blood glucose and insulin, while a ketogenic diet is one focused on reducing the amount of total carbohydrates. Ketogenic diets suppress appetite [112] and are utilized as a dietary intervention to promote weight reduction in patients with obesity [10]. Some reports suggest that the association of glycemic index/load of foods and health outcomes and obesity is equivocal [113,114]. While the hyperinsulinemia with insulin resistance may increase sympathetic nervous system activity (and potentially increase blood pressure) and facilitate fat cell lipolysis, the effects of insulin resistance on resting metabolic rate (beyond the associated increase in fat mass) are unlcear. Nonetheless, other reports support high glycemic index/load dietary intake is indeed associated with an increased risk of type 2 diabetes mellitus, metabolic syndrome, and cardiovascular disease [115], and that low glycemic index/load dietary patterns are associated with decreased incidence of diabetes mellitus and cardiovascular disease [116]. Furthermore, in the specific, yet illustrative case of gestational diabetes mellitus, low glycemic index diets reduce the risk of insulin use and reduce the risk of macrosomia [117]. If a low-carbohydrate diet facilitates weight reduction, then this is likely due to decreased hunger, reduced energy intake, and spontaneous increase in physical activity [116], with possible mitigation of the decrease in muscle mass and resting metabolic rate often found with weight reduction. Finally, foods high in glycemic index may be associated with abdominal obesity in susceptible individuals and populations [118], which may have clinical implications for populations genetically susceptible to abdominal obesity (e.g., Asians) [119] and populations who favor intake of high glycemic index foods (i.e., rice) [17].

When food intake is prompted by hunger, food intake is favored when hormones that increase hunger exceed the effects of hormones that decrease hunger (or increase satiety) [9,27]. However, food intake is often due to factors beyond physiologic hunger, such as appetite cues (i.e., food marketing and body senses of sight, sound, smell, taste, and touch) [11]. Other factors that influence type and amount of food intake include meal timing and emotions, environment, reward, mental stress, psychiatric disease, and eating disorders [11] Sleep restriction often increases hunger, appetite, food intake, and visceral fat, with the increase in caloric intake more than the energy requirements of extended wakefulness [120,121]. Information and education gaps may exist that affect "calories in," such as an inadequate understanding of nutrition, misinterpretation of food labels, lack of reporting of the nutritional content of foods (e.g., in some restaurants), and misleading marketing messages (e.g., "low fat," "multigrain," "no added sugar," "natural sugar," "cholesterol free") [10] Some obesogenic medications can increase hunger, while anti-obesity medications can decrease hunger [12,27]. Other interventions that can affect "calories in" include impaired carbohydrate intestinal absorption such as through alpha glucosidase inhibitors (i.e., acarbose) and impaired fat intestinal absorption such as through gastrointestinal lipase inhibitors (e.g., orlistat). Finally, nutrient absorption can be affected by the microbiome, as well as restriction of food intake and/or reduced absorptive intestinal endothelial surface area (i.e., some bariatric procedures) [9].

Regarding "calories out," variances exist in the thermogenic effect of food, individual resting metabolic rate, and individual physical activity (i.e., physical exercise, non-exercise activity thermogenesis). Medications can help excrete energy, such as glucose urinary excretion via sodium glucose transporter 2 inhibitors. Supplements can affect uncoupling proteins, thus facilitating increased heat loss during enzymatic reactions [12]. Brown and beige fat cells have higher concentration of mitochondria that promote greater generation of heat than white fat [8]. Pregnancy and lactation increase resting metabolic rate, which utilizes a greater proportion of food energy than non-pregnant and non-lactating individuals. Conversely, routine physical exercise with the same muscles induces adaptations leading to increased skeletal muscle efficiency, weight reduction induces adaptations leading to reduced metabolic rate, and both would be expected to utilize a less proportion of food energy [8]. Sleep disruption does not appear to affect RMR or TEF [122]. Overall, whether it be consumed or stored macronutrients, the simple statement of "calories in equals calories out" is only clinically meaningful with an understanding of the complexities of "calories in" and "calories out", as well as the metabolic efficiencies and inefficiencies noted in Fig. 9.

3.2.5. ***MMO #12:*** *obesity is caused by eating processed foods*

Some processing is required for food safety. However, many foods are highly "processed" in a way that makes them more energy dense, less nutrient dense, more efficiently absorbed in the intestine, and generally less healthful in patients with overweight and obesity [123]. This is especially a concern in areas of the world experiencing the obesity epidemic. Unprocessed, processed, and ultra-processed foods often differ in nutritional value [124,125]. Unprocessed (or minimally processed) foods are mostly unaltered (often termed "whole foods"). That said, some processing of foods is often necessary to make foods more healthful. For example, foods are often "processed" prior to being sold or eaten [e.g., frozen, canned, smoked, dried, baked, or pasteurized (i.e., treated with mild heat to kill pathogens such as bacteria)]. Other examples of healthful food processing include ensuring the food is edible (e.g., harvesting grain, shelling nuts, slaughtering livestock for food), as well as cooking, freezing, and packaging (e.g., cans). Examples of processed foods often considered healthful include olive oil from olives, and dark chocolate [126].

While some processing can make food more healthful, ultra-processing can make foods less healthful. Ultra-processed foods often undergo changes that often enhance caloric density and taste (i.e., add sugar, fat, and/or artificial flavor), enhance visual appeal (i.e., add artificial color), and alter food content and structure (e.g., remove micronutrients and reduce fiber content). Examples include many white breads, sweetened breakfast cereals, instant noodles, chicken or fish nuggets (with added breading, salt, and fat), cured meats (soaked in salt/brine, nitrates, and sometimes sugar), chocolate bars, candy, flavored and salted chips, and sweetened beverages [124,125]. Energy dense ultra-processed foods contribute to obesity, cardiovascular disease, and increased mortality [123,127–130]. Ultra-processed foods often have greater caloric density, more efficient gastrointestinal absorption, and less micronutrients and fiber. Consuming ultra-processed foods often results in greater consumption of carbohydrates and fats, and thus greater consumption of calories [123].

The degree of food processing is reflected in the NOVA (not a reported acronym) classification system, which groups foods according to the extent and purpose of industrial processing [125]. Not all authors support the clinical utility of such classification [131]. Nonetheless, the type and degree of food processing can affect the healthfulness of foods. Especially in areas of the world experiencing the obesity epidemic, foods are made

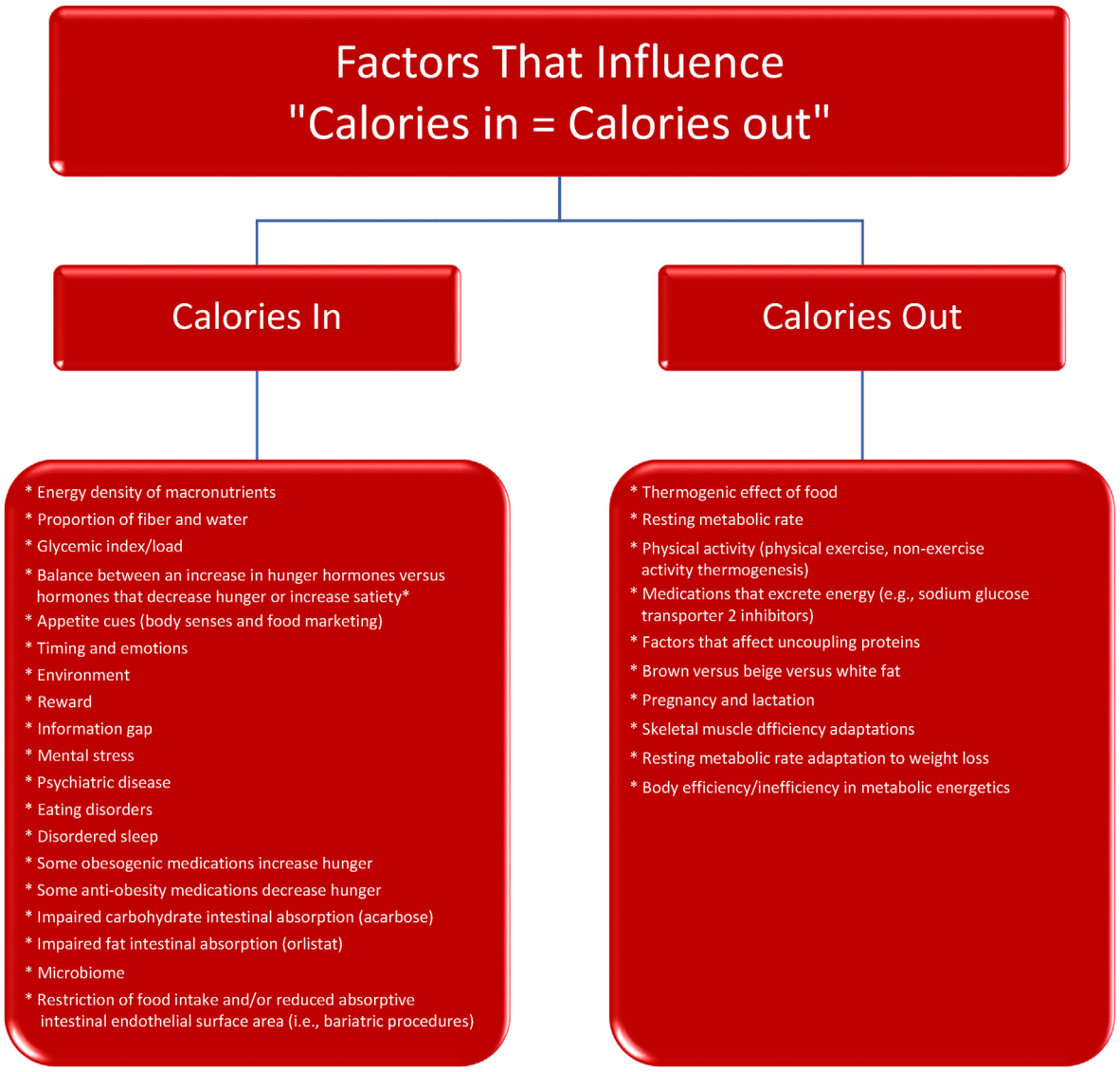

Fig. 9. Factors involved in "Calories in Equals Calories Out." Beyond the physics, clinical application of "Calories In and Calories Out" requires consideration of the complexities of multiple factors applicable to management of obesity [8,9,11,27].
* Gastrointestinal hormones that may increase hunger include ghrelin and neuropeptide Y; gastrointestinal hormones that may decrease hunger/increase satiety include somatostatin, cholecystokinin, motilin, insulin, glucagon, pancreatic polypeptide, glucagon like peptide-1, oxyntomodulin, fibroblast growth factor 19, peptide YY, and amylin [9].

less healthful when they undergo "ultra-processing" to be more energy dense, when fiber and micronutrients are removed, and when foods are produced with added sugar, sweeteners, fat, and/or salt. In summary, while some food processing is often desirable, many ultra-processed foods not only increase the risk of overweight, obesity, cardiometabolic risk factors, type 2 diabetes mellitus cardiovascular disease, cancer, irritable bowel syndrome, depression, frailty conditions, and all-cause mortality [132]. The dangers of ultra-processed foods are amplified when the consumption of ultra-processed unhealthful foods promote addictive-like eating of the same unhealthful foods [133].

3.2.6. ***MMO #13:*** *obesity is caused by breakfast patterns*

"Breakfast" is defined by the time of day (first meal of the day, usually in the morning), and not by its quantitative, caloric, and qualitative content. The health effects of breakfast may differ between adults and younger persons [134,135]. But even among adults, breakfast is often characterized as "the most important meal of the day." A lack of routine breakfast is associated with an increase in cardiometabolic risk and cardiovascular disease [136–138]. One of the behaviors reported by those who have achieved long-term weight reduction is that they routinely eat breakfast (The National Weight Control Registry http://www.nwcr.ws/).

These favorable reports are somewhat countered by other studies that suggest increased daily caloric consumption may promote weight gain among those assigned to eat breakfast versus those assigned to not eat breakfast. Meta-analyses of randomized trials suggest insisting patients eat breakfast may not always be a good strategy for weight reduction [139]. Conceptually, it may be challenging to claim that skipping a single breakfast is harmful, given the often favorable data regarding the effects of intermittent fasting and time restricted eating [10].

That said, it is unclear that clinically meaningful body weight differences occur with daily breakfast versus skipping breakfast. Those who eat breakfast may have a compensatory increase in physical activity later in the day, while those who do not eat breakfast may have a compensatory increase energy intake later in the day [140]. Except for possible increased insulin sensitivity with breakfast, health outcomes may not differ to a clinically meaningful degree among adults who eat breakfast versus those who do not eat breakfast [140].

From the standpoint of caloric balance and clinically meaningful chances in body weight, what may matter most to patient health are the circumstances of skipping breakfast, the healthful content of the breakfast, and how it affects total daily energy consumption. Lack of desire for breakfast may suggest night-time eating disorder, which may contribute to increased net total daily caloric intake [11,72]. Regarding breakfast content, not all breakfasts are alike, and not all breakfast food intake has the same clinical implications. For example, especially in patients with obesity, dyslipidemia, and hypertension, a daily breakfast consisting of ultra-processed meats, ultra-processed carbohydrates, and energy dense saturated fats containing >1000 Calories and >2000 mg of sodium would be expected to be less healthful than a daily breakfast consisting of Greek yogurt, oatmeal, berries and/or nuts containing <200 Calories and <100 mg sodium) [30,141]. (For clarity, 1000 calories equal 1kilocalorie, which is the most reported energy measure. If the "C" is capitalized in "Calorie," then that is equal to 1000 calories or one kilocalorie or kcal). For some patients, skipping an unhealthful breakfast might be more beneficial than consuming an unhealthful breakfast. In summary, eating breakfast may very well be important for many individuals being treated for obesity; however, this may depend on the caloric and nutritional content of the breakfast. Recommendations regarding breakfast illustrate the potential benefits of individualizing medical nutrition therapy.

3.2.7. ***MMO #14:*** *obesity is commonly caused by pathogens in the intestine (microbiome)*

The ileum and colon contain approximately 100 trillion organisms (bacteria, fungi, and viruses), with trillions being bacteria [142]. The microbiota composition of the microbiome may influence caloric balance, with some intestinal bacteria promoting increased density of small intestinal villi capillaries, thus allowing for more efficient absorption of nutrients than other bacteria [9]. Gram positive Firmicutes may more efficiently extract calories from carbohydrates (via fermentation) than Gram negative Bacteroidetes [143]. Intestinal bacteria may also affect energy balance via central nervous system [144] and other body organ signaling, including crosstalk with adipose tissue [145]. Intestinal bacteria can also affect bile acid metabolism and gut hormone secretion; both which affect energy balance [9]. Finally, microbiota may have epigenetic effects (e.g., DNA methylation, histone modifications, and non-coding RNA expression) through signaling from microbiota-derived metabolites (e.g., short-chain fatty acids), which may alter intestinal permeability, immune responses, inflammatory reactions, and insulin resistance [146].

Conceptually, unless due to a pathogenic infection, then the gut microbiome might often best be considered neither intrinsically healthful nor unhealthful. The clinical implications of an individual's microbiome and its function are dependent upon the presentation of the individual. Malnourished individuals who are underweight may benefit from microbiota that promote more efficient absorption of nutrients. Overnourished individuals with pre-obesity or obesity may not benefit, and may be harmed, from microbiota that promote more efficient absorption of nutrients. A common example of an intervention that may alter the microbiome includes the use of antibiotics, (i.e., including antibiotics transmitted via animal feed), which may reduce the diversity of microbiota, and potentially contribute to obesity [147]. Conversely, in patients with obesity, bariatric surgery may alter the microbiome in a manner that reduces the efficiency of extracting calories from consumed carbohydrates [148].

For most individuals, obesity is a multifactorial disease. The clinical results of studies of the effects of fecal transplant in humans with obesity differ compared to studies done in rodents. For example, fecal microbiota transplantation from lean individuals to patients (humans) with obesity has not yet consistently led to a reduction in body mass index, despite changes in the intestinal microbiome and bile acid profiles more like the lean donor [149]. Thus currently, the utility of microbiota-based therapies as treatment remains uncertain and the use of microbiome restoration for obesity might best be restricted to research settings [150].

3.2.8. ***MMO # 15:*** *obesity is due to a lack of access to plant-based foods*

"Food deserts" can be defined as regions of the country that often feature large proportions of households with low incomes, inadequate access to transportation, and a limited number of food retailers providing fresh produce and healthy groceries for affordable prices (https://www.ers.usda.gov/webdocs/publications/45014/30940_err140.pdf). About 10% of census tracts in the United States are identified as food deserts (e.g., 13.5 million people or about 5% of the US population). https://www.usda.gov/. Perhaps even more insidious than food deserts are so-called "food swamps," which are areas with a high-density of establishments selling high-calorie fast food and junk food, relative to more healthful food options. The related term of "food security" is sometimes used to reflect not just the availability, but also the accessibility/affordability of nutrition foods. Conversely, "food insecurity" is sometimes used to identify the lack of access to affordable, nutritious food, which may affect as much as ~12% of US households [151]. Potential solutions to increase availability to more healthful foods are zoning laws that simultaneously restrict access to unhealthy food outlets and incentivize healthy food retailers to locate in underserved neighborhoods [152].

Given that obesity affects 42% of US adults and given that only about 5% of US individuals live in areas identified as food deserts, it is unlikely that lack of proximity to plant-based foods is a cause of obesity for most individuals with obesity. In fact, although still low compared to omnivores, the percent of vegetarians and vegans is actually increasing [153]. This is likely at least partially because of increasing evidence that healthful plant-based diets are associated with reduced rates of obesity, heart disease, cancer, and possibly all-cause mortality [154]. Yet, despite an increase in the rate of vegetarians, the obesity epidemic continues to increase. A potential explanation is that the health benefits of a plant-based diet are negated when more healthful plant based whole foods (i.e., with natural fiber and nutrients) are replaced by plant based ultra-processed foods, fried foods, and refined carbohydrates [10].

In an illustrative example, approximately 40% of the population of India is vegetarian (300–400 million individuals) [155]. Despite a high percent of vegetarians, the prevalence of obesity in India is 40%, with the highest prevalence in South India (47%) [156]. Understanding that refined and ultra-processed vegetarian diets can be unhealthful helps explain the apparent paradoxical finding that vegetarian dietary patterns can be associated with a high incidence of obesity [157]. Additionally, those from South Asia are especially at increased (not decreased risk) for increase in central obesity, visceral fat, and cardiovascular disease [119], which may be influenced by common culturally driven intake of plant-based foods, such as white rice [17].

Overall, the limitation of healthful plant-based food among those living in food deserts and foods swamps is important, and is a priority to enhance health, lengthen life, and reduce illness, disability, and health disparities [151]. However, food deserts and food insecurity only apply to a minority of people in the US. Little evidence exists that lack of access to plant-based foods is the major cause of obesity for most individuals. A more prevalent challenge is the nutritional content of food intake. Practical, culturally-based nutritional guidance can help ensure that when plant-based diets are consumed, they are healthful [17,119,158].

3.2.9. ***MMO #16****: lack of breastfeeding for a full 2 years is a major sole cause of unalterable obesity in offspring*

The health benefits of breastfeeding are not a myth. However, breastfeeding often presents challenges for the mother with obesity, which may be exacerbated by worry, shame, and guilt. Animal studies support mother's milk as containing macronutrients, micronutrients, antibodies, growth factors and hormones that potentially benefit lifelong human health, reducing the predisposition for obesity, metabolic disease, cardiovascular diseases, and neurobehavioral disorders [159]. Human milk provides immunity support, unique nutrients, and other bioactive factors important for infants during early stages of development [160]. Children fed human breast milk:

- Have a lower risk of developing obesity-related metabolic consequences, possibly due to favorable epigenetic influences (i.e., alterations in gene expression without alteration in the genetic code sequencing) [161,162].
- Have a microbiome more resistant to obesity [160].
- More healthful taste/food preferences [163].
- Overall lower risk of developing obesity [164], which is an effect potentially diminished when breast milk is fed from a bottle, instead of directly from the breast [165].

Sibling-pair and intervention studies suggest moderate evidence supporting that ever, compared with never, consuming human milk is associated with a lower risk of overweight and obesity, with a lack of sufficient evidence to fully define the relationship between the duration of any human milk consumption and the risk of future overweight and/or obesity in offspring [166]. Systemic reviews and meta-analyses support breastfeeding as reducing the risk of overweight or obesity, even when corrected socioeconomic status and publication bias [167,168]. The American Academy of Pediatrics (AAP) recommends exclusive breastfeeding for approximately 6 months after birth, along with healthful complementary foods introduced at about 6 months, as long as mutually desired by mother and child for 2 years or beyond [164].

Thus, when possible, exclusive breastfeeding is generally recommended for at 6 months and along with complementary foods 2 or more years after infant birth [164,169,170]. Reports support [171] and challenge [172] the degree that that breastfeeding promotes postpartum weight loss. That said, challenges exist regarding the universal adoption of breastfeeding, such as among minority populations [173]. Additionally, breast feeding beyond 6 months is not normalized in all areas, with persistent adverse stigma, lack of partner/family support, and presence of workplace barriers. Some mothers are unable to produce enough milk, especially mothers with obesity. Mothers with obesity may have delayed lactogenesis, lower prolactin responses to suckling, and are prone to early cessation of breastfeeding [174]. When mothers with obesity can produce milk, the composition of the milk may differ compared to lean mothers, having potential implications for breastfed offspring [175].

Clinical interactions with mothers with obesity may be more productive when clinicians avoid communications that further the adverse stigma of obesity; communications are best redirected towards healthful, well-informed lifestyle choices [176]. The breastfeeding recommendations noted above are illustrative of a well-informed health choice. Nonetheless, if breastfeeding did not occur for longer than 6-months, then the mother might reasonably be reassured that 6-month breastfeeding does provide benefits to the child [177]. If the mother with obesity could not, or did not breastfeed at all, then it may be unproductive to focus on assigning blame or imparting excessive guilt to a mother who may already have these feelings due to having obesity. Furthermore, it is unlikely that the lack of adequate breastfeeding will prove to be the sole "cause" of a predictable, unalterable, and predestined life-long state of obesity for the child. Instead, lack of breastfeeding may be one of many potential factors that may be applicable to multifactorial disease that is obesity [30]. Rather than a focus on blame or reinforcement of guilt in the new mother with obesity who did not breastfeed for the recommended full 2 years (or not at all), the postpartum period could be viewed as an opportunity to implement achievable postpartum weight management [178]. Implementation of healthful nutrition and routine physical activity for the post-partum mother may favorably affect the offspring, given that parental food habits and feeding strategies are the most dominant determinants of a child's eating behavior and food choices [179], and given that parents play a critical role in developing and shaping their children's physical activity [180].

3.3. Diagnosis

3.3.1. ***MMO #17:*** *increased subcutaneous adipose tissue is healthy; increased visceral adipose tissue is unhealthy*

Peripheral subcutaneous adipose tissue (SAT) can be healthy, when it provides physical padding, thermal insulation, and unfettered energy stored in peripheral SAT during positive caloric balance, mitigating energy overflow to other fat depots (e.g., visceral and epicardial fat) and other body organs (e.g., muscle and liver) [4,48,54]. When adipocyte proliferation and differentiation is impaired in peripheral SAT, then this may result in energy overflow to other fat depots and other body organs, which contributes to metabolic and cardiovascular disease. Abdominal SAT is a component of android fat, and at minimum, its deep component is considered pathogenic (not "healthy" or "protective") [121]. SAT is often 80% or more of body fat mass, with most of potentially pathogenic adipose tissue-derived free fatty acids in both the systemic circulation and portal circulation originating from SAT [181,182]. Beyond SAT metabolic dysfunction that may contribute to sick fat or adiposopathy, an increase in SAT often contributes to fat mass disease (e.g., sleep apnea, skin friction, and musculoskeletal abnormalities potentially leading to immobility) which is unhealthy, not healthy.

Visceral adipose tissue (VAT) is potentially protective by providing storage of energy, physical padding to abdominal organs, and thermal insulation [4,48,54]. VAT is potentially pathogenic with higher basal lipolysis than SAT, increased sensitivity to catecholamines, decreased sensitivity to insulin, and direct access to the liver, all resulting in greater potential of endocrinopathies and immunopathies compared to SAT. That said, SAT and VAT mass and function are interdependent, with the accumulation of android and VAT reflective of global adipose tissue dysfunction (adiposopathy) [4,48,54,121,182]. Overall, the interdependent functions of SAT and VAT support the rationale to consider global adipose tissue function when assessing the adverse health consequences of obesity, rather than a focus on a somewhat artificial separation of the interconnected pathogenic potential of SAT and VAT.

3.3.2. ***MMO #19:*** *individuals with obesity have low metabolism. Lean people are "naturally skinny" because they have a higher metabolism*

Unless accompanied by sarcopenia, individuals with obesity generally have an increase in both fat and muscle mass compared to lean individuals. Among patients with obesity, muscle mass and absolute maximum muscle strength is often increased compared to those without obesity, likely because adiposity acts as a chronic overload stimulus on the larger antigravity muscles (e.g., quadriceps and calf), thus increasing muscle size and strength [183]. The increase in body tissue (muscle or fat) increases the resting metabolic rate ("metabolism") required to sustain the increase in body tissue cellular functions. The greater the amount of body tissues, the greater the resting metabolic rate, helping to explain why many individuals with obesity have higher resting metabolic rates than lean individuals [184–186].

Conversely, weight reduction reduces resting metabolic rate [187]. The correlation between the amount of body tissue and the resting metabolic rate is consistent with formulas developed to estimate resting metabolic rate. Resting metabolic rate can be measured by direct and indirect calorimetry [8]. However, resting metabolic rate can be estimated by formulas such as the Harris-Benedict and Mifflin St. Jeor Equation, that in addition to age and genetic sex, also includes weight and height (i.e., with weight and height also used to calculate body mass index) – again emphasizing the direct correlation between body mass and resting metabolic rate [8,188].

Some patients believe their obesity is because they have "low metabolism" However, when tested objectively, patient sense of having a low or high metabolic rate does not correlate to actual resting metabolic rate

[189]. When compared to control groups, individuals with apparent diet-resistance obesity and "low metabolism" do not have a reduction in total energy expenditure, basal energy expenditure, or sleeping energy expenditure [190].

That said, variances in metabolic rates do exist [191], for reasons such as genetic influences (See Fig. 5). Patients with obesity and metabolic syndrome may have lower resting metabolic rate [192]. However, even then, adults with lower basal metabolic rates may not gain more weight over time than adults with higher basal metabolic rate, implying that variances in food intake or physical activity counterbalance variations in basal metabolic rate as a risk factor for weight gain [193]. Overall, individuals with obesity typically have higher absolute resting energy expenditure and total energy expenditure. The evidence does not support that obesity is sustained by a lower daily energy expenditure or lower resting energy expenditure [194].

None of this is to suggest that resting metabolic rate is without clinical relevance. Changes in resting metabolic rate are highly relevant during weight reduction among patients treated for obesity. During times of weight reduction, both tissue loss (i.e., fat and muscle reduction) and metabolic adaptations contribute to a reduction in resting metabolic rate [195]. The reduction in resting metabolic rate with weight reduction makes further weight reduction more challenging, and at minimum, may increase the length of time necessary to achieve weight reduction goals [196].

Another consideration is body composition. For most individuals, it is the increase in fat mass that is most pathogenic. For the same body mass index, an individual with higher fat mass will have a greater risk for adiposopathic "fat mass disease" and "sick fat disease." (See Section 3.1.1) In contrast to an *increase* in fat mass that contributes to ill health, it is the *decrease* in muscle mass that may lead to sarcopenia, which has adverse health outcomes (e.g., reduced locomotion, frailty, reduced quality of life, osteoporosis, worsening metabolic health, and possibly an increase in obesity) [197]. Factors that contribute to sarcopenia include genetic predisposition, unhealthful nutrition or malnutrition, physical inactivity, chronic illness (especially with cachexia), neuro-degenerative diseases, hormone changes (e.g., hypercortisolism, abnormal thyroid function), medications, immobility, zero gravity, weight cycling, and age [198,199]. Sarcopenia often accompanies not only an increase in percent body fat, but also a reduction in bone mineral density, sometimes termed osteosarcopenic obesity syndrome [200]. Regarding prevalence, in an evaluation of patients evaluated for arthroplasty, 6.4% had sarcopenic obesity [201].

Within the context of obesity management, perhaps the most clinically relevant scenario affecting body mass (and thus body metabolism) is that weight reduction is usually accompanied by a reduction in both fat and muscle. In other words, when patients treated for obesity undergo longitudinal body composition analyses, it is common to find that patients lose both fat and muscle. This equates to a reduction in resting metabolic rate due to loss of body tissues and metabolic adaptations. The ability to maintain or increase muscle mass during hypocaloric weight reduction is highly challenging. Potential strategies to mitigate skeletal muscle mass reduction during active weight reduction include higher intakes of protein, and increased physical exercise, especially resistance training [202,203]. To avoid unrealistic expectations and potential disappointment, patients undergoing weight reduction might best be informed that during weight reduction, some loss of lean body mass is expected. It is true that in some circumstances, patients with obesity may engage in a medical nutrition plan and a rigorous physical exercise program that successfully reduces fat and preserves or even increases lean body mass. While this outcome is rare, when such success does occur, then the clinician should consider acknowledging this achievement via discussion of the body composition analysis with the patient. Positive interactions with the clinicians may be motivational in promoting further goal setting [204].

Another challenge encountered in the clinical practice of obesity medicine is when patients undergo weight cycling. Some highly trained athletes "cycle" through periods of heavy and sustained physical exercise and caloric restrictions prior to competitions. After competition, these athletes may slowly increase caloric intake to maintain muscle mass and increase resting metabolic rate (sometimes termed "reverse dieting") [205]. More commonly, cyclical weight reduction occurs among non-athletes who do not engage in muscle sparing or muscle building activity. Such individuals have an increased risk of reducing their muscle mass [199] and developing sarcopenia.

Finally, given the tenuous correlation between resting metabolic rate and obesity, some patients may inquire what other factors may better help explain the apparent differences between individuals regarding energy balance and fat accumulation. Along with genetic/epigenetic, biological (increased proportion of brown adipogenesis), and environmental factors, one of the greatest variances in energy expenditure among individuals is non-exercise activity thermogenesis (NEAT). Variances in NEAT can range between 150 and 500 kcal per day, which is often greater than the amount of daily physical exercise [79] (See Section 3.2.2). As noted in section 3.2.4, total energy expenditure is typically:

- 70% resting metabolic rate (RMR)
- 20% physical activity [exercise activity thermogenesis (EAT) and non-exercise activity thermogenesis (NEAT)]
- 10% diet-induced thermogenesis (DIT)

Given that many patients with obesity have limited EAT, and given the wide variability in NEAT, then this variance in NEAT may help explain much of the otherwise unexplainable interindividual variances in body fat accumulation. NEAT includes "fidgeting," occupation physical activity, leisure time activity, sitting, standing, toe-tapping, shoveling, playing the guitar, dancing, singing, and washing [206]. While some may consider non-physical exercise walking as part of NEAT, the Obesity Medicine Association includes any walking in its physical activity goals (i.e., at least 5000 steps per day) [8,10]. Section 3.2.2 provides examples of behavior changes that may increase NEAT, and thus favorably affect energy balance among patients with obesity.

3.3.3. ***MMO #19:*** *"big boned" individuals have no potential to achieve a healthy body weight*

When patients claim to be "big boned," this can be interpreted in several ways. "Big boned" might refer to larger individuals based upon height, with increased height correlating to increased mass of many body tissues. Given that body mass index (BMI) is calculated by weight in kilograms divided by height in meters squared, then for the same weight, a taller person will have a reduced calculated BMI (not increased BMI) compared to a shorter person.

Regarding percent body fat, the 2019 US Army Standards of Medical Fitness (https://armypubs.army.mil/epubs/DR_pubs/DR_a/pdf/web/ARN8673_AR40_501_FINAL_WEB.pdf) has established acceptable percent body fat metrics, utilizing waist and neck circumference and height for men, and waist, neck, and hip circumference and height for women (https://www.omnicalculator.com/health/army-body-fat). If all other metrics remained the same, then an increase in height calculates to a decrease in percent body fat for both men and women, not an increase in percent body fat.

"Big boned" might refer to larger body framed individuals. However, little evidence supports that larger body frame promotes increased body fat [207–209].

Finally, "big boned" might conceivably refer to bone mineral density (BMD). The discussion of the relationship between obesity and BMD is an opportunity to discuss another obesity myth. A common belief is that obesity is always associated with an increase in BMD. Perhaps this belief is because an increase in muscle mass is often described among patients with obesity, attributable to chronic overload on larger antigravity muscles [183]. If muscle mass is increased due to increased resistance to the musculoskeletal system, then one would expect such individuals would have an increase in BMD. Some reports do support that individuals

with increasing obesity have increasing BMD [210,211], but only up until a body mass index of ~50 kg/m^2, where an inflection point occurs and BMD may begin to decrease for some (e.g., women and Black individuals) [211].

Conversely, other studies suggest that among those below 60 years of age, fat mass has a moderate, negative association with BMD most notable in men at high levels of body fat; with lean mass having a strong positive association with BMD [212]. A takeaway message may be that increased lean body mass/muscle in younger individuals seems to consistently correlate to increased bone mass [213–218]. Conversely, worsening physical inactivity coupled with an aging population may help explain why the rate of sarcopenic obesity is increasing [219]. It may also help explain the emergence of the "osteosarcopenia," describing when the low bone mass and deterioration of the micro-architecture of the bone found with osteoporosis, concurrently occurs with the loss of muscle mass, strength and function found with sarcopenia [220].

Finally, irrespective of the perception of the degree bone size, bone weight contributes only a small amount to overall body weight. At least regarding the mineral portion, ash weight of bone contributes a minor amount to total body weight (~3–10 pounds) [221].

3.4. Treatment

3.4.1. ***MMO #20:*** *low-fat diets are the best way to reduce body fat*

The rationale supporting low fat diets for patients with obesity may initially be compelling. Fats have more concentrated stored energy (kilocalories per gram) than either carbohydrates or protein. Fat-containing foods are often energy dense. Fats have a lower TEF than carbohydrates/proteins. Saturated fats and trans fats are associated with increased risk of cardiovascular disease and cancer [10]. Thus, it seems reasonable to recommend low-fat diets as the preferred medical nutrition therapy for patients with obesity. With specific regard to cholesterol, the reduced-fat Therapeutic Lifestyle Changes (TLC) Diet (promoted by the National Cholesterol Education Program, Adult Treatment Panel) was commonly used in earlier lipid-altering drug clinical trials [10], and still sometimes used in current lipid clinical trials. It may therefore seem intuitive that if eating dietary fat increases body fat (and blood lipids), then reducing dietary fat would reduce body fat.

However, clinical science and clinical experience suggest that accumulation of body fat is due to more than the consumption of dietary fats (See Fig. 9.). Universal recommendation of low-fat diet for all patients may have potential adverse health consequences [222]. Some have suggested that: "The low-fat ideology came to dominate America in the last decades of the 20th century and subsequently contributed to an excess intake of refined carbohydrates which, in the context of an increasingly sedentary lifestyle, may have fueled the obesity epidemic" [223]. Given that cardiovascular disease and cancer are the most common cause of death among adults with obesity, it may be relevant that the diet plan perhaps having the greatest evidence of long-term health benefits would be the Mediterranean Diet [10,158]. This emphasizes the point that, while not considered "low fat," consumption of a healthful diet containing healthful fats (e.g., mono and polyunsaturated fats) has among the best evidence of a reduction in the risk for cardiovascular disease [158] and reduction in the risk of cancer [224].

With advancements in clinical science and clinical experiences, clinicians now have a better understanding that obesity is a multifactorial disease best managed by an individual, patient-centered approach. Nutritional factors related to improved health outcomes among patients with obesity include interventions that are evidenced based, that consider both quantitative and qualitative content of food, and that prioritize patient agreement and adherence. At least in the short-term, carbohydrate and calorie restricted nutritional intervention may result in greater weight reduction than fat and calorie restricted nutritional intervention [225]. Overall, a "low fat diet" may very well be the best medical nutrition therapy for some patients. But no single medical nutritional therapy is uniformly optimal or appropriate for everyone. Simply because a "diet" is low fat, or plant-based, does not necessarily make it healthful (See Section 3.2.8). Multiple evidenced-based dietary interventions are available [10,158]. The best medical nutrition therapy is a patient-centric one, based upon the patient's clinical presentation, and the patient's agreement and willingness to adhere to an evidenced-based dietary plan [10].

3.4.2. ***MMO #21:*** *nutrition medical therapy is more effective when based upon patient preference*

For any medical nutrition therapy to be effective, the patient needs to agree to the treatment plan and be willing to adhere to the treatment plan. Once consent is given to implement an evidenced-based medical nutrition therapy, then meta-analyses suggest that patient preference in weight reduction strategies have no significant effect on duration or attrition, with greater weight reduction often occurring in the control groups [226]. While possibly counterintuitive, randomized clinical trials do not support improved weight reduction when based upon patient food preference [227,228]. In summary, nutritional factors related to improved outcomes include:

- Qualitative considerations (e.g., macronutrients and micronutrients)
- Quantitative (e.g., fiber, energy density, energy intake)
- Patient agreement to evidenced-based medical nutrition therapy and adherence to the dietary plan

With specific regard to dietary and other preferences, effective change sometimes requires choices and behavior that differ from what patients would prefer to do, and/or have historically done [11].

3.4.3. ***MMO #22:*** *vitamins and herbal supplements are effective in achieving weight reduction*

Vitamins are micronutrient organic molecules derived from plant and animal foods, and necessary for metabolic processes, such as serving as a non-protein facilitator (coenzyme) for protein enzymes. Supplements are defined as substances taken in addition to dietary intake, such as concentrated forms of a nutrient (e.g., vitamins), isolated formulations of a nutrient (e.g., herbs or botanicals), minerals, and amino acids [12]. Consuming concentrated vitamin preparations do not promote weight reduction. Little evidence supports herbal, mineral, or amino acid supplements as safely providing clinically meaningful weight reduction accompanied by long-term health outcome benefits [12]. The Obesity Medicine Association has not endorsed the clinical use of any supplement and has published a dedicated Clinical Practice Statement regarding "Concomitant medications, functional foods, and supplements" [12].

3.4.4. ***MMO #23:*** *After implementing implementing a 500 Calorie daily energy deficit diet, then as long as this daily energy deficit is maintained, fat weight reduction will continue to occur indefinitely according to the calculation that 3500 Calories are stored per pound of fat*

In individuals with moderate physical inactivity, 70% of energy expenditure is due to resting metabolic rate and 10% due to diet-induced thermogenesis [229]. Only 20% of daily energy expenditure is often due to physical activity. Regarding physical activity, a gross estimate is that it takes an additional 10,000 steps per day per week to "burn" an additional 3500 Calories (kcal) per week, which is the approximate amount of energy found in one pound of fat. Depending on the body mass index of the individual, walking on a level treadmil for 20 minutes may may "burn" less than 100 Calories [230]. Admittedly, figures such as these are highly simplified. They are not adjusted for the weight of the individual, nor adjusted for the potential metabolic and skeletal muscle adaptations with chronic physical exercise and/or incline/decline terrain of the walk. As long as these limitations are understood, then the clinical application of these number figures highlight the challenges of solely relying upon physical activity as the only intervention employed towards body fat reduction in patients with obesity.

That said, the commonly cited 3500 Calories per pound of fat is blatantly misleading in how it is often applied to predicting the effects of

long-term body weight effects of energy deficits (i.e., hypocaloric dietary intake or increase in physical activity). The 3500-kcal number figure is an estimated calculation (i.e., Wishnofsky's Rule), that during time of its development, was "in striking agreement with the value of 3700 kcal obtained" from computations based on adipose tissue samples [231]. The challenges with this calculation are multifold:

- The first phases of many hypocaloric weight reduction nutritional intervention typically include a reduction in the body's glycogen pool (i.e., mainly from skeletal muscle), and its associated water (i.e., each gram of glycogen is stored with at least 3 grams of water [232]). It is the substantial loss of body water due to depletion of glycogen stores that helps explains why the most rapid weight reduction with dietary interventions usually occur at the beginning of a hypocaloric metabolic nutrition therapy, and perhaps especially so with a low-carbohydrate ketogenic diet [233]. This rapid and sometimes substantial initial weight reduction is not predominantly fat weight reduction. It is this misunderstanding, and possible exploitation of this misunderstanding, that helps account for the promotion of the apparent success of many "weight loss foods" (e.g., grapefruit, pineapple, apple, and cucumber diets) and other "miracle fat-burning diets," whose initial weight reduction is mostly due to a decrease in muscle glycogen/mass and dehydration, and not body fat reduction [234].
- Another major misapplication of the "3500 kcal per pound of fat" calculation is the assertion that a set daily caloric deficit will have perpetual cumulative effects. (See Fig. 10). An illustrative example would be that a daily caloric deficit of 500 kcal would be expected to reduce body fat by one pound per week (7 days × 500 kcal = 3500 kcal) – presumably continued indefinitely. However, any caloric deficit from baseline should always be compared to the baseline caloric value, and not perpetually subtracted over time. For clinicians who find this line of thinking clinically challenging might best frame the discussion in terms of going from a baseline caloric intake of 2000 Calories per day (as an example) to 1500 Calories per day, rather focus on a potentially misunderstood perpetually subtracted 500 Calorie per day deficit.
- Beyond potential errors in mathematical application, weight reduction due to body tissue loss (fat or muscle) decreases resting metabolic rate and facilitates metabolic adaptations, resulting in a new body weight energetic setpoint. This is clinically manifest by a weight reduction plateau, limiting further body weight reduction over time [231] unless accompanied by additional caloric deficits in intake or increases in energy expenditure.

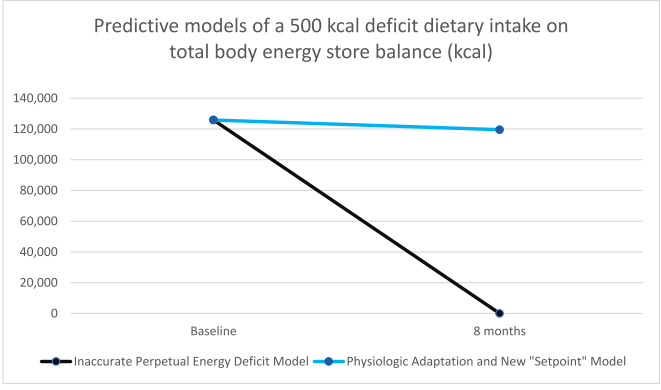

Fig. 10. Inaccurate perpetual energy deficit model versus physiologic adaptation and new "setpoint" model. This figure describes an adult human male weighing 66 kg (145 pounds) and who has total body energy stores of 125,822 kcal [235]. Assuming this adult human male is consuming 2000 kcal per day, then if this individual were to consume 500 kcal less per day, then the perpetual energy deficit model would predict the absurd notion this adult male would consume his entire body caloric body mass at 251 days (125,822/500) or about 8 months, despite a dietary intake of 1500 kcal per day. Conversely, the physiologic adaptation and new setpoint model might predict that a new daily caloric intake of 1500 kcal per day would result in about 5% non-water weight reduction (and thus a 5% reduction in total body energy stores), followed by a plateau and new setpoint at around 6 months determined by the patient's new energy balance [236]. This figure has acknowledged limitations in its calculations for the purpose of simplicity. Its intent is not precision in number figures, but rather to highlight the fallacy of the perpetual energy deficit model.

Table 7
Calories expended per hour of exercise.

Activity for one hour	Calories expended
Walking 3.5 miles per hour (mph)	314
Running 5 mph	606
Elliptical (moderate intensity)	365
Bicycling < 10 mph	292
Aerobics (low impact)	365
Swimming laps (moderate intensity)	423

Shown are approximate calorie expenditures for a person weighing 160 lbs [230].

3.4.5. ***MMO #24:*** *increased physical exercise is the most effective way to reduce weight*

In most cases, a nutritional caloric deficit is required for clinically meaningful weight reduction. Physical exercise modestly contributes to weight reduction. Table 7 shows the calories expended for an individual weighing 160 lbs (73 kg) exercising for 1 h [230]. The caloric expenditures for 1 h of these common physical exercise activities range between 300 and 600 kcal. For reference, one slice of 14-inch regular crust pepperoni pizza may contain approximately 300 kcal. Despite the modest energy expenditure for these common activities, the benefits of routine physical activity go well beyond affects upon body weight (See Table 8.).

Table 8
Illustrative benefits of routine physical activity/exercise.

Body weight and composition:	**Metabolic benefits:**
• Facilitates weight reduction • Helps maintain weight reduction • May increase muscle mass • May reduce percent body fat	• Improve insulin sensitivity • Reduce hyperglycemia • Improve blood lipids
Cardiovascular benefits:	**Cancer benefits:** [5]
• Decrease sympathethic activity • Decrease blood pressure • Reduce heart rate • Reduce risk for cardiac dysrhythmias • Improve autonomic balance • Enhance fibrolysis • Enhance coronary dilation capacity • Facilitate myocardial cellular regeneration • Increase myocardial oxygen utilization • Improve endothelial function • Reduce myocardial and plaque inflammation	• Reduce risk of cancer onset • Reduce risk of cancer recurrence • Inhibits cancer cell proliferation • Increase cancer cell apoptosis • Reduce inflammation • Enhance effectiveness of cancer treatment • Counteract cancer and cancer treatment complications
Sleep benefits:	**Neuromusculoskeletal benefits**:
• Reduce time to sleep • Reduce wake time during nighttime • Reduce daytime sleepiness • Possible reduction in sleep medications	• Improve muscle strength • Improve bond strength • Improve balance and coordination • Reduce risk of dementia • Reduce depression • Reduced anxiety & improved mood

Beyond its favorable effects on body weight and body composition, routine physical activity has multiple health benefits applicable to the patient with obesity [10].

For example, in patients with obesity, a major potential body weight benefit is that routine physical activity/exercise is among the most validated determinants of weight reduction maintenance [28]. Routine physical exercise may help with weight reduction maintenance, and counter-weight reduction adaptations that otherwise result in potential weight regain through the following mechanisms [237].

- Decreased hunger
- Increase satiety
- Increased leptin sensitivity
- Increased insulin sensitivity
- Decrease in adipose tissue denovo lipogenesis
- Preservation of muscle and its beneficial metabolic processes (fat oxidation)

3.4.6. ***MMO #25:*** *every 1 pound of muscle that replaces fat burns an additional 50 calories per day*

An often-stated axiom suggests that if 10 pounds of muscle are gained and replace 10 pounds of fat, then resting energy expenditure will increase 500 kcal per day. However, muscle and fat are two different body tissues. Muscle or fat vary independently. Although both are from mesodermal origin, from a cellular/tissue standpoint, muscle and fat do not "replace" one another. Increased physical exercise does not turn fat into muscle tissue; lack of physical exercise does not turn muscle into fat tissue.

Table 9
Approximate resting energy expenditure of adult body organs [238].

Organ or tissue	Daily metabolic rate (kcal/kg/day)	Daily metabolic rate (kcal/pound/day)	Body organ weight	Total energy expenditure (kcal/day)
Skeletal Muscle	13	6	20 kg/44 lbs (female)	260 (female)
			30 kg/66 lbs (male)	390 (male)
Adipose tissue	4.5	2	13 kg/28 lbs (female)	59 (female)
			16 kg/35 lbs (male)	72 (men)
Liver	200	91	1.5 kg/3.31 lbs	300
Brain	240	109	1.3 kg/2.87 lbs	312
Heart	440	200	0.3 kg/0.66 lbs	132
Kidney	440	200	0.13 kg/0.29 lbs (per kidney)	114 (per 2 kidneys)
Remaining body mass*	12	5	27.24 kg/60 lbs (female)	327 (female)
			30.6 kg/67.3 lbs (male)	368 (male)
Total resting energy expenditure				~1500 (female) ~1700 (male)

Body organ mass varies among individuals, especially skeletal muscle and adipose tissue. The values above represent values for lean individuals. Some patients with obesity may have hundreds of pounds of body fat, with a corresponding increase in resting energy expenditure to sustain the increased adipose tissue organ cellular activity. In a lean individual, lean body mass (LBM) is ~75% of total body mass (TBM); skeletal muscle is ~40% of TBM. A lean man with a TBM of 175 lbs may have ~131 lbs LBM, and ~70 lbs of skeletal muscle. * Remaining body mass: skin, intestines, bones, and lungs.

A confounder may be the reports that many body builders consume 4000 Calories or more per day. This may give the impression that skeletal muscle requires vastly higher resting energy than adipose tissue. As can be seen from Table 9, the daily energy expenditure of resting muscle is not as different from adipose tissue as many might believe. If 10 pounds of fat is lost, and 10 pounds of muscle is gained, then the resting energy expenditure would be expected to increase by only about 40 kcal per day (60 extra kcal per day from 10 lbs of added muscle, less the 20 kcal per day from 10 lbs of lost adipose tissue). That said, Table 8 describes benefits of routine physical activity, including how resistance training can help increase percent of lean body mass. For patients with overweight or obesity, losing 10 pounds of fat and gaining 10 pounds of muscle promotes a healthier metabolic and musculoskeletal body composition. Furthermore, during negative caloric balance, resistance training can be especially important in mitigating muscle loss and limit the reduction in resting metabolic rate. Table 9 shows approximate resting energy expenditure of adult body organs [238].

3.4.7. ***MMO #26:*** *access to exercise equipment, gym memberships, and physical activity trackers will result in weight reduction*

Access to physical exercise equipment may help facilitate weight reduction if the equipment is accessed and used; wearable technology may facilitate weight reduction if the technology is worn and viewed. Unfortunately, over 50% of new gym members will abandon activities before the 3rd month; less than 5% may remain for more than 12 months [239]. Wearable technologies may not provide additional long-term benefit among groups already receiving standard behavioral intervention [240,241]. The benefits of physical activity trackers may be specific to the individual, with greater potential benefits possibly in middle to older age adults [242,243].

That said, wearable devices for physical activity intervention may be useful for preventing and treating obesity in children and adolescents [244]. The facilitation of longer-term weight reduction with wearable technologies may also be time dependent, with greater efficacy if used for 12 weeks or more [245]. In summary, the success of gym memberships and health wearable devices for weight reduction among patients with overweight and obesity is highly dependent upon the individual and the actual use of the gym or wearable technology. Health wearable devices may be effective intervention tools/strategies for reducing body weight and body mass index in individuals with overweight/obesity and chronic comorbidities, with accelerometer/pedometers and commercial health wearable technologies potentially effective even without accompanying counseling [246,247].

3.4.8. ***MMO #27:*** *setting more "realistic" obesity goals will ultimately achieve greater weight reduction than more aggressive goals*

Setting goals that are neither attainable nor safe has little rationale as effective behavior therapy. The components of the often-used SMART approach to goal setting are ***S***pecific, ***M***easurable, ***A***ssignable, ***R***ealistic, and ***T***ime-Related [11]. Thus, treatment goals should be balanced, with avoidance of goal setting beyond the patient's ability. That is because goals that are too aggressive may be discouraging and promote disengagement and abandonment of weight reduction strategies. Conversely, adjustment of patient goals to only modest outcomes may undermine optimism and motivation for engaging in behaviors required for clinically meaningful weight reduction. It is true some evidence supports that overly aggressive weight reduction goals (i.e., that are less "realistic") predict higher attrition and less success with weight reduction; however, other studies support better weight reduction outcomes with more aggressive weight reduction goals [30]. In fact, some reports suggest that for patients with obesity, the benefits of higher motivation via higher goals outweighs the concern that high goals may undermine effort [248]. Seemingly "unrealistic" targets may actually improve weight reduction results [249]. Overall, while goal setting is important, the success of a weight reduction strategy requires a patient-centered, individualized, multifactorial approach that includes frequent encounters with medical

professionals, education, stimulus control, cognitive restructuring, self-monitoring, behavioral contracting, problem solving, social support, reinforcement contingencies, and other behavior interventions that are doable, efficacious, measurable, and that incorporate self-ownership [11].

3.4.9. ***MMO #28:*** *small favorable changes in nutritional intake and physical activity will yield large long-term benefits; slow and gradual weight reduction is ultimately more effective than large and rapid weight reduction*

Older dietary literature warned against rapid weight reduction, as it was thought to contribute to ill health and/or greater chance of weight regain. However, clinical trial evidence supports that the greater and more rapid the initial weight reduction, the greater the long-term weight reduction maintenance [30]. The prescribing information of many anti-obesity medications suggest that if there is no clinical improvement (e.g., at least 4–5% reduction of baseline body weight) after 12–16 weeks with one anti-obesity medication, then the clinician should consider using alternative anti-obesity medications or increasing the anti-obesity medication dose (if applicable) [27]. The point being that the degree of early success or early lack of success with weight reduction interventions may be predictive of its long-term success. In a study of 1.4 million users and weight reduction goals with a popular activity online tracking application, "high amounts of early weight loss, which some researchers have classified as unsustainable, leads to higher goal achievement rates" [250].

3.4.10. ***MMO #29:*** *efforts to reduce body weight in patients with obesity is unhealthy, because the weight will inevitably return, and fluctuations in body weight (e.g., yo-yo dieting) are more dangerous than maintaining a high body weight*

Weight reduction in patients with obesity improves health outcomes (See Table 10). Interventions regarding nutrition [10], physical activity [10], behavior modification, pharmacotherapy [27], and bariatric surgery [9] are successful in improving not just the weight of many patients, but the health of patients as well [251]. Yo-yo dieting, or weight cycling, describes recuring weight reduction followed by weight regain over time in the same patient. Dangers of weight cycling include sarcopenic obesity [199] and increased in cardiometabolic risk [252]. The caveat is that at least when studied in rodents, weight cycling or yo-yo dieting may be more healthful than no dieting at all [253]. The essential message is that while repeated "yo yo dieting" may have adverse health effects, attempts to achieve a healthy body weight should not be avoided for fear of less-than-optimal results. With regard to addressing the potential causes of body fat regain, an overall helpful message might be [254]:

> *Weight loss awakens the body's defense system in a manner that is persistent, saturated with redundancies, and well-focused on the objective of restoring the body's depleted energy reserves. Successful, long term weight loss requires recognition of the strength and persistence of these biological pressures, and a better understanding of how they may be countered with environmental, behavioral, pharmaceutical, or other interventions. To be effective, interventions aimed at preventing weight regain will likely need to be as comprehensive, persistent, and redundant as the biological adaptations they are attempting to counter [255].*

3.4.11. ***MMO #30:*** *drugs should not be used to treat obesity, because obesity is due to unhealthful diet and lack of exercise and because weight will only be regained once anti-obesity medications are discontinued. Bariatric surgery is the "easy way out," a procedure reserved for patients who are failures and "cheaters," and is a procedure too dangerous for everyone else*

In the earlier days of treatment for diabetes mellitus, hypertension, and dyslipidemia, skepticism (if not bias) existed against medication treatment for diseases thought to be due to unhealthful lifestyle. Earlier treatments for diabetes mellitus, hypertension, and dyslipidemia were often poorly tolerated, sometimes unsafe, and did not initially have evidence of improved cardiovascular outcomes or mortality [27]. Currently, many treatments for diabetes mellitus, hypertension, and dyslipidemia are efficacious, generally well tolerated, have proven cardiovascular and mortality benefits, and represent "standards of care." [27].

Today, bias exists against medication treatment for obesity, often thought to be due to an unhealthful lifestyle. Earlier anti-obesity agents were often ineffective, poorly tolerated, sometimes unsafe, and had no evidence of improved cardiovascular outcomes or mortality. Newer approved and investigational anti-obesity agents are more efficacious, better tolerated, safer, and may soon have clinical outcomes trial evidence for improved cardiovascular outcomes and perhaps mortality [27]. Regarding need for lifelong treatment for a lifelong disease, the disease of obesity is no different than other chronic metabolic diseases such as type 2 diabetes mellitus, hypertension, and dyslipidemia. In most cases, chronic medications are no longer effective in helping to control chronic diseases if the medications are discontinued (See Fig. 11.). Both anti-obesity medications and bariatric procedures have proven health benefits [9,27]. The reasons for the low degree of drug treatment for obesity and low degree of bariatric surgery (See Fig. 12.) are multifactorial, including bias as evidenced by the failure to recognize and treat obesity as a disease. (See Section 3.1.1)

Table 10
Potential benefits of weight reduction in patients with obesity [3].

1.	Healthful nutrition (including negative caloric balance in patients with obesity) and regular physical activity often improve anatomic, physiologic, inflammatory, and metabolic body processes
2.	Medically managed weight reduction in patients with obesity often improves glucose and lipid metabolism, reduces blood pressure, and reduces the risk of thrombosis
3.	Medically supervised weight management programs for patients with obesity have the potential for statistically significant and clinically meaningful weight loss maintenance
4.	Weight reduction in patients with obesity may reduce premature all-cause mortality
5.	Weight reduction in patients with obesity may have favorable cardiac hemodynamic effects
6.	Weight reduction in patients with obesity may improve obstructive sleep apnea and osteoarthritis
7.	Weight reduction in patients with obesity may reduce the onset of certain cancers, improve response to cancer treatments, and reduce the onset/recurrence of new cancers
8.	Weight reduction in females with obesity may improve metabolism (polycystic ovary syndrome) as well as improve obesity-related gynecologic and obstetric disorders; weight loss in males with obesity may increase testosterone levels when hypogonadism is due to the adiposopathic consequences of obesity
9.	Weight reduction in patients with obesity may improve quality of life, improve body image, and improve symptoms of some psychiatric disorders (e.g., depression)
10.	Weight loss in males and childbearing females with pre-obesity or obesity may help mitigate epigenetically transmitted increased risk of obesity and metabolic disease in future generations

Weight reduction in patients with obesity has multiple potential health benefits in patients with obesity.

4. Conclusions

This Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) on obesity myths, misunderstandings, and/or oversimplifications is one of a series of OMA CPSs designed to assist clinicians better understand the physiology and pathophysiology of obesity, as well as the integration of published OMA CPS. Knowledge of these common issues obesity may help clinicians and patients improve the management of the disease of obesity.

Transparency [258]

This manuscript was derived and edited from the 2021 Obesity Medicine Association (OMA) Obesity Algorithm. Beginning in 2013,

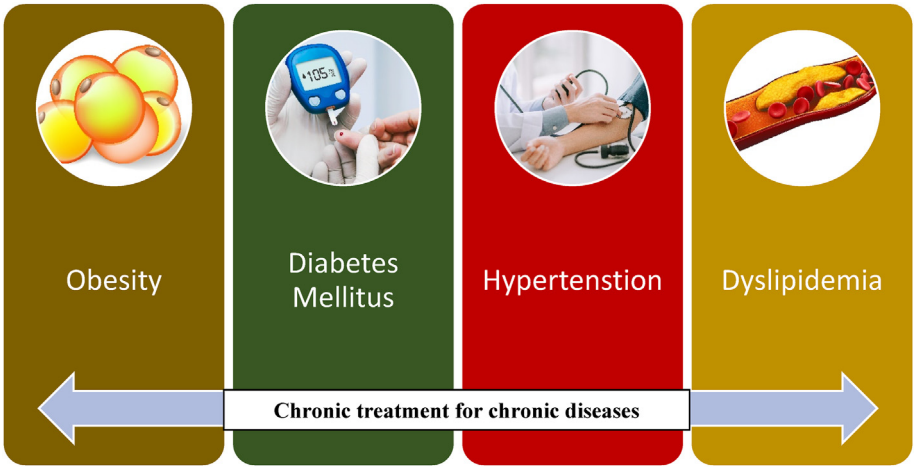

Fig. 11. Obesity, diabetes mellitus, hypertension, and dyslipidemia are all chronic diseases that require chronic treatment. In each case, treatment typically includes healthful nutrition, routine physical activity, behavior modification, medications, and possibly bariatric surgery. If these chronic metabolic diseases are well-controlled on medication, then stopping the medication will likely cause the chronic disease to be less well-controlled.

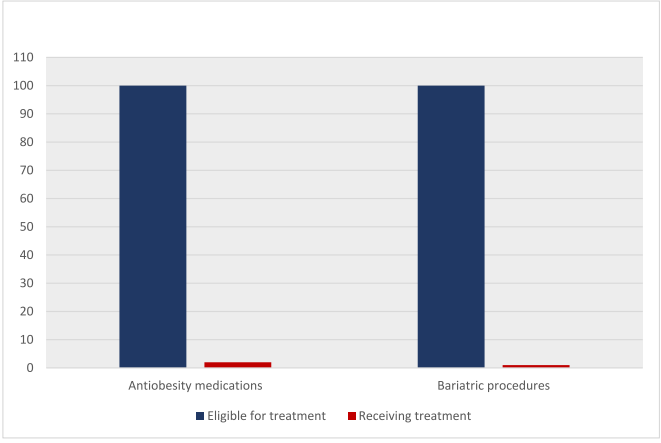

Fig. 12. US percent comparison of patients *eligible* for antiobesity medication and bariatric surgery versus those *receiving* antiobesity medication and bariatric procedures such as surgical treatment. The total eligible to receive anti-obesity medication is shown as 100%. The percent of eligible patients treated with anti-obesity medication is 2% [256]. The total eligible to receive bariatric surgery is shown as 100%. The percent of eligible patients treated with bariatric surgery is 1% [257].

OMA created and maintained an online Adult "Obesity Algorithm" (i.e., educational slides and eBook) that underwent yearly updates by OMA authors and was reviewed and approved annually by the OMA Board of Trustees. This was followed by a similar Pediatric "Obesity Algorithm," with updates approximately every two years by OMA authors. Authors of prior years' version of the Obesity Algorithm are included in Supplement #1.

Group composition

Over the years, the authors of the OMA Obesity Algorithm have represented a diverse range of clinicians, allied health professionals, clinical researchers, and academicians. (Supplement #1) The authors reflect a multidisciplinary and balanced group of experts in obesity science, patient evaluation, and clinical treatment.

Author contributions

HEB re-wrote the initial draft derived from the 2021 Obesity Algorithm; HEB, AG, and JT reviewed, edited, and approved the document.

Managing disclosures and dualities of interest

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Individual Disclosures

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Evidence

The content of the OMA Obesity Algorithm and this manuscript is supported by citations, which are listed in the References section.

Ethics review

This OMA Clinical Practice Statement manuscript was peer-reviewed and approved by the OMA Board of Trustee members prior to publication. Edits were made in response to reviewer comments and the final revised manuscript was approved by all the authors prior to publication. This submission did not involve human test subjects or volunteers.

Conclusions and recommendations

This Clinical Practice Statement is intended to be an educational tool that incorporates the current medical science and the clinical experiences

of obesity specialists. The intent is to better facilitate and improve the clinical care and management of patients with pre-obesity and obesity. This Clinical Practice Statement should not be interpreted as "rules" and/or directives regarding the medical care of an individual patient. The decision regarding the optimal care of the patient with pre-obesity and obesity is best reliant upon a patient-centered approach, managed by the clinician tasked with directing an individual treatment plan that is in the best interest of the individual patient.

Updating

It is anticipated that sections of this Clinical Practice Statement may require future updates. The timing of such an update will depend on decisions made by Obesity Pillars Editorial team, with input from the OMA members and OMA Board of Trustees.

Disclaimer and limitations

Both the OMA Obesity Algorithms and this Clinical Practice Statement were developed to assist health care professionals in providing care for patients with pre-obesity and obesity based upon the best available evidence. In areas regarding inconclusive or insufficient scientific evidence, the authors used their professional judgment. This Clinical Practice Statement is intended to represent the state of obesity medicine at the time of publication. Thus, this Clinical Practice Statement is not a substitute for maintaining awareness of emerging new science. Finally, decisions by practitioners to apply the principles in this Clinical Practice Statement are best made by considering local resources, individual patient circumstances, patient agreement, and knowledge of federal, state, and local laws and guidance.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.obpill.2022.100034.

References

[1] Bays HE, McCarthy W, Burridge K, Tondt J, Karjoo S, Christensen S, Ng J, Golden A, Davisson L, Richardson L. Obesity Algorithm eBook. 2021. presented by the Obesity Medicine Association, www.obesityalgorithm.org. https://obesitymedicine.org/obesity-algorithm/.
[2] Chaput JP, Ferraro ZM, Prud'homme D, Sharma AM. Widespread misconceptions about obesity. Canadian family physician Medecin de famille canadien 2014;60(973–5):81–4.
[3] Fitch AK, Bays HE. Obesity definition, diagnosis, bias, standard operating procedures (SOPs), and telehealth: an Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) 2022. Obesity Pillars 2022;1:100004.
[4] Bays H. Adiposopathy, "sick fat," Ockham's razor, and resolution of the obesity paradox. Curr Atherosclerosis Rep 2014;16:409.
[5] Lazarus E, Bays HE. Cancer and obesity: an obesity medicine association (OMA) clinical practice statement (CPS) 2022. Obesity Pillars 2022;3:100026.
[6] Ullah R, Rauf N, Nabi G, Yi S, Yu-Dong Z, Fu J. Mechanistic insight into high-fat diet-induced metabolic inflammation in the arcuate nucleus of the hypothalamus. Biomed Pharmacother 2021;142:112012.
[7] Bays H, Scinta W. Adiposopathy and epigenetics: an introduction to obesity as a transgenerational disease. Curr Med Res Opin 2015;31:2059–69.
[8] Burridge K, Christensen SM, Golden A, Ingersoll AB, Tondt J, Bays HE. Obesity history, physical exam, laboratory, body composition, and energy expenditure: an Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) 2022. Obesity Pillars 2022;1:100007.
[9] Shetye B, Hamilton FR, Bays HE. Bariatric surgery, gastrointestinal hormones, and the microbiome: an obesity medicine association (OMA) clinical practice statement (CPS) 2022. Obesity Pillars 2022;2:100015.
[10] Alexander L, Christensen SM, Richardson L, Ingersoll AB, Burridge K, Golden A, et al. Nutrition and physical activity: an obesity medicine association (OMA) clinical practice statement 2022. Obesity Pillars 2022;1:100005.
[11] Freshwater M, Christensen S, Oshman L, Bays HE. Behavior, motivational interviewing, eating disorders, and obesity management technologies: an Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) 2022. Obesity Pillars 2022;2:100014.
[12] Tondt J, Bays HE. Concomitant medications, functional foods, and supplements: an obesity medicine association (OMA) clinical practice statement (CPS) 2022. Obesity Pillars 2022;2:100017.
[13] Heindel JJ, Blumberg B. Environmental obesogens: mechanisms and controversies. Annu Rev Pharmacol Toxicol 2019;59:89–106.
[14] Shahnazaryan U, Wójcik M, Bednarczuk T, Kuryłowicz A. Role of obesogens in the pathogenesis of obesity. Medicina (Kaunas) 2019;55.
[15] Kitahara CM, Flint AJ, Berrington de Gonzalez A, Bernstein L, Brotzman M, MacInnis RJ, et al. Association between class III obesity (BMI of 40-59 kg/m2) and mortality: a pooled analysis of 20 prospective studies. PLoS Med 2014;11:e1001673.
[16] Carr KA, Epstein LH. Choice is relative: reinforcing value of food and activity in obesity treatment. Am Psychol 2020;75:139–51.
[17] Bays HE, Ng J, Sicat J, Look M. Obesity pillars roundtable: obesity and east Asians. Obesity Pillars 2022;2:100011.
[18] Haines MS, Leong A, Porneala BC, Meigs JB, Miller KK. Association between muscle mass and diabetes prevalence independent of body fat distribution in adults under 50 years old. Nutr Diabetes 2022;12:29.
[19] Butcher JT, Mintz JD, Larion S, Qiu S, Ruan L, Fulton DJ, et al. Increased muscle mass protects against hypertension and renal injury in obesity. J Am Heart Assoc 2018;7:e009358.
[20] Han TS, Al-Gindan YY, Govan L, Hankey CR, Lean MEJ. Associations of body fat and skeletal muscle with hypertension. J Clin Hypertens 2019;21:230–8.
[21] Fyfe JJ, Hamilton DL, Daly RM. Minimal-dose resistance training for improving muscle mass, strength, and function: a narrative review of current evidence and practical considerations. Sports Med 2022;52:463–79.
[22] Polyzos SA, Margioris AN. Sarcopenic obesity. Hormones (Basel) 2018;17:321–31.
[23] Wang M, Tan Y, Shi Y, Wang X, Liao Z, Wei P. Diabetes and sarcopenic obesity: pathogenesis, diagnosis, and treatments. Front Endocrinol 2020;11:568.
[24] Silveira EA, da Silva Filho RR, Spexoto MCB, Haghighatdoost F, Sarrafzadegan N, de Oliveira C. The role of sarcopenic obesity in cancer and cardiovascular disease: a synthesis of the evidence on pathophysiological aspects and clinical implications. Int J Mol Sci 2021:22.
[25] Magkos F, Fraterrigo G, Yoshino J, Luecking C, Kirbach K, Kelly SC, et al. Effects of moderate and subsequent progressive weight loss on metabolic function and adipose tissue biology in humans with obesity. Cell Metabol 2016;23:591–601.
[26] Ryan DH, Yockey SR. Weight loss and improvement in comorbidity: differences at 5%, 10%, 15%, and over. Curr Obesity Rep 2017;6:187–94.
[27] Bays HE, Fitch A, Christensen S, Burridge K, Tondt J. Anti-obesity medications and investigational agents: an obesity medicine association (OMA) clinical practice statement (CPS) 2022. Obesity Pillars 2022:100018.
[28] Varkevisser RDM, van Stralen MM, Kroeze W, Ket JCF, Steenhuis IHM. Determinants of weight loss maintenance: a systematic review. Obes Rev : Off J Int Assoc Study Obesity 2019;20:171–211.
[29] Ramage S, Farmer A, Eccles KA, McCargar L. Healthy strategies for successful weight loss and weight maintenance: a systematic review. Appl Physiol Nutr Metabol 2014;39:1–20.
[30] Casazza K, Fontaine KR, Astrup A, Birch LL, Brown AW, Bohan Brown MM, et al. Myths, presumptions, and facts about obesity. N Engl J Med 2013;368:446–54.
[31] Magkos F. On adaptive thermogenesis: just another weight-loss tale? Am J Clin Nutr 2020;112:1157–9.
[32] Martins C, Roekenes J, Salamati S, Gower BA, Hunter GR. Metabolic adaptation is an illusion, only present when participants are in negative energy balance. Am J Clin Nutr 2020;112:1212–8.
[33] Coutinho SR, Rehfeld JF, Holst JJ, Kulseng B, Martins C. Impact of weight loss achieved through a multidisciplinary intervention on appetite in patients with severe obesity. Am J Physiol Endocrinol Metab 2018;315:E91–8.
[34] Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-Being 2021;16:1862481.
[35] Phelan SM, Burgess DJ, Yeazel MW, Hellerstedt WL, Griffin JM, van Ryn M. Impact of weight bias and stigma on quality of care and outcomes for patients with obesity. Obes Rev : Off J Int Assoc Study Obesity 2015;16:319–26.
[36] Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci 2020:21.
[37] Singh S, Shankar R, Singh GP. Prevalence and associated risk factors of hypertension: a cross-sectional study in urban Varanasi. Int J Hypertens 2017;2017:5491838.
[38] Kopin L, Lowenstein C. Dyslipidemia. Ann Intern Med 2017;167:ITC81–96.
[39] Muir LA, Neeley CK, Meyer KA, Baker NA, Brosius AM, Washabaugh AR, et al. Adipose tissue fibrosis, hypertrophy, and hyperplasia: correlations with diabetes in human obesity. Obesity 2016;24:597–605.
[40] Wadden TA, Considine RV, Foster GD, Anderson DA, Sarwer DB, Caro JS. Short- and long-term changes in serum leptin dieting obese women: effects of caloric restriction and weight loss. J Clin Endocrinol Metab 1998;83:214–8.
[41] Farias MM, Cuevas AM, Rodriguez F. Set-point theory and obesity. Metab Syndr Relat Disord 2011;9:85–9.
[42] Smith KB, Smith MS. Obesity Statist Primary care 2016;43:121–35. ix.

[43] Yu E, Ley SH, Manson JE, Willett W, Satija A, Hu FB, et al. Weight history and all-cause and cause-specific mortality in three prospective cohort studies. Ann Intern Med 2017;166:613–20.
[44] Khan SS, Ning H, Wilkins JT, Allen N, Carnethon M, Berry JD, et al. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. JAMA Cardiol 2018;3:280–7.
[45] Wade KH, Carslake D, Sattar N, Davey Smith G, Timpson NJ. BMI and mortality in UK biobank: revised estimates using mendelian randomization. Obesity 2018;26:1796–806.
[46] Global BMIMC, Di Angelantonio E, Bhupathiraju Sh N, Wormser D, Gao P, Kaptoge S, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. Lancet 2016;388:776–86.
[47] Berrington de Gonzalez A, Hartge P, Cerhan JR, Flint AJ, Hannan L, MacInnis RJ, et al. Body-mass index and mortality among 1.46 million white adults. N Engl J Med 2010;363:2211–9.
[48] Bays HE. Adiposopathy is "sick fat" a cardiovascular disease? J Am Coll Cardiol 2011;57:2461–73.
[49] Caleyachetty R, Thomas GN, Toulis KA, Mohammed N, Gokhale KM, Balachandran K, et al. Metabolically healthy obese and incident cardiovascular disease events among 3.5 million men and women. J Am Coll Cardiol 2017;70:1429–37.
[50] Iliodromiti S, Celis-Morales CA, Lyall DM, Anderson J, Gray SR, Mackay DF, et al. The impact of confounding on the associations of different adiposity measures with the incidence of cardiovascular disease: a cohort study of 296 535 adults of white European descent. Eur Heart J 2018;39:1514–20.
[51] Lavie CJ, Laddu D, Arena R, Ortega FB, Alpert MA, Kushner RF. Healthy weight and obesity prevention: JACC health promotion series. J Am Coll Cardiol 2018;72:1506–31.
[52] Schulze MB. Metabolic health in normal-weight and obese individuals. Diabetologia; 2018.
[53] Jung CH, Lee WJ, Song KH. Metabolically healthy obesity: a friend or foe? Korean J Intern Med 2017;32:611–21.
[54] Lavie CJ, De Schutter A, Parto P, Jahangir E, Kokkinos P, Ortega FB, et al. Obesity and prevalence of cardiovascular diseases and prognosis-the obesity paradox updated. Prog Cardiovasc Dis 2016;58:537–47.
[55] Mongraw-Chaffin M, Foster MC, Kalyani RR, Vaidya D, Burke GL, Woodward M, et al. Obesity severity and duration are associated with incident metabolic syndrome: evidence against metabolically healthy obesity from the multi-ethnic study of atherosclerosis. J Clin Endocrinol Metab 2016;101:4117–24.
[56] Caballero B. Humans against obesity: who will win? Adv Nutr 2019;10:S4–s9.
[57] Tirthani E, Said MS, Rehman A. Genetics and obesity. StatPearls. Treasure island (FL). StatPearls Publishing; 2022. Copyright © 2022, StatPearls Publishing LLC.
[58] Shi Y, Zhang H, Huang S, Yin L, Wang F, Luo P, et al. Epigenetic regulation in cardiovascular disease: mechanisms and advances in clinical trials. Signal Transduct Targeted Ther 2022;7:200.
[59] Hinney A, Hebebrand J. Polygenic obesity in humans. Obes Facts 2008;1:35–42.
[60] Loos RJF, Yeo GSH. The bigger picture of FTO: the first GWAS-identified obesity gene. Nat Rev Endocrinol 2014;10:51–61.
[61] Zarza-Rebollo JA, Molina E, Rivera M. The role of the FTO gene in the relationship between depression and obesity. A systematic review. Neurosci Biobehav Rev 2021;127:630–7.
[62] Nagrani R, Foraita R, Gianfagna F, Iacoviello L, Marild S, Michels N, et al. Common genetic variation in obesity, lipid transfer genes and risk of Metabolic Syndrome: results from IDEFICS/I.Family study and meta-analysis. Sci Rep 2020;10:7189.
[63] Iwamoto SJ, Grimstad F, Irwig MS, Rothman MS. Routine screening for transgender and gender diverse adults taking gender-affirming hormone therapy: a narrative review. J Gen Intern Med 2021;36:1380–9.
[64] Hafeez H, Zeshan M, Tahir MA, Jahan N, Naveed S. Health care disparities among lesbian, gay, bisexual, and transgender youth: a literature review. Cureus 2017;9:e1184.
[65] Kyinn M, Banks K, Leemaqz SY, Sarkodie E, Goldstein D, Irwig MS. Weight gain and obesity rates in transgender and gender-diverse adults before and during hormone therapy. Int J Obes 2021;45:2562–9.
[66] Escobar-Morreale HF, Álvarez-Blasco F, Botella-Carretero JI, Luque-Ramírez M. The striking similarities in the metabolic associations of female androgen excess and male androgen deficiency. Hum Reprod 2014;29:2083–91.
[67] Wiik A, Andersson DP, Brismar TB, Chanpen S, Dhejne C, Ekström TJ, et al. Metabolic and functional changes in transgender individuals following cross-sex hormone treatment: design and methods of the GEnder Dysphoria Treatment in Sweden (GETS) study. Contemp Clin Trials Commun 2018;10:148–53.
[68] Connelly PJ, Marie Freel E, Perry C, Ewan J, Touyz RM, Currie G, et al. Gender-affirming hormone therapy, vascular health and cardiovascular disease in transgender adults. Hypertension 2019;74:1266–74.
[69] Elbers JMH, Asscheman H, Seidell JC, Megens JAJ, Gooren LJG. Long-term testosterone administration increases visceral fat in female to male Transsexuals1. J Clin Endocrinol Metab 1997;82:2044–7.
[70] Amianto F, Ottone L, Abbate Daga G, Fassino S. Binge-eating disorder diagnosis and treatment: a recap in front of DSM-5. BMC Psychiatr 2015;15:70.
[71] Rushing JM, Jones LE, Carney CP. Bulimia nervosa: a primary care review. Prim Care Companion J Clin Psychiatry 2003;5:217–24.
[72] Stunkard AJ, Allison KC, Geliebter A, Lundgren JD, Gluck ME, O'Reardon JP. Development of criteria for a diagnosis: lessons from the night eating syndrome. Compr Psychiatr 2009;50:391–9.
[73] Pope L, Hansen D, Harvey J. Examining the weight trajectory of college students. J Nutr Educ Behav 2017;49:137–41. e1.
[74] Gutin I. Educational differences in mortality associated with central obesity: decomposing the contribution of risk and prevalence. Soc Sci Res 2020;90:102445.
[75] Mohajeri MH, Brummer RJM, Rastall RA, Weersma RK, Harmsen HJM, Faas M, et al. The role of the microbiome for human health: from basic science to clinical applications. Eur J Nutr 2018;57:1–14.
[76] Periasamy M, Herrera JL, Reis FCG. Skeletal muscle thermogenesis and its role in whole body energy metabolism. Diabetes Metab J 2017;41:327–36.
[77] Rosenbaum M, Heaner M, Goldsmith RL, Christian Schulze P, Shukla A, Shen W, et al. Resistance training reduces skeletal muscle work efficiency in weight-reduced and non-weight-reduced subjects. Obesity 2018;26:1576–83.
[78] Barclay CJ. The basis of differences in thermodynamic efficiency among skeletal muscles. Clin Exp Pharmacol Physiol 2017;44:1279–86.
[79] Chung N, Park MY, Kim J, Park HY, Hwang H, Lee CH, et al. Non-exercise activity thermogenesis (NEAT): a component of total daily energy expenditure. J Exercise Nutr biochem 2018;22:23–30.
[80] Tucker LA, Parker K. 10-Year weight gain in 13,802 US adults: the role of age, sex, and race. J Obesity 2022;2022:7652408.
[81] Hubáček JA. Eat less and exercise more - is it really enough to knock down the obesity pandemia? Physiol Res 2009;58(1):S1–s6.
[82] Howell S, Kones R. Calories in, calories out" and macronutrient intake: the hope, hype, and science of calories. Am J Physiol Endocrinol Metab 2017;313:E608–12.
[83] Rolls BJ. Dietary energy density: applying behavioural science to weight management. Nutr Bull 2017;42:246–53.
[84] Hindrichsen IK, Kreuzer M, Madsen J, Bach Knudsen KE. Fiber and lignin analysis in concentrate, forage, and feces: detergent versus enzymatic-chemical method. J Dairy Sci 2006;89:2168–76.
[85] Venter R. Ruminants and termites have something in common? Stockfarm 2015;5:31.
[86] Zhong H, Zhou J, Abdelrahman M, Xu H, Wu Z, Cui L, et al. The effect of lignin composition on ruminal fiber fractions degradation from different roughage sources in water buffalo (Bubalus bubalis). Agriculture 2021;11:1015.
[87] Dhingra D, Michael M, Rajput H, Patil RT. Dietary fibre in foods: a review. J Food Sci Technol 2012;49:255–66.
[88] Drewnowski A, Maillot M, Vieux F. Multiple metrics of carbohydrate quality place starchy vegetables alongside non-starchy vegetables, legumes, and whole fruit. Front Nutr 2022;9:867378.
[89] Torres-Carot V, Suárez-González A, Lobato-Foulques C. The energy balance hypothesis of obesity: do the laws of thermodynamics explain excessive adiposity? Eur J Clin Nutr 2022.
[90] Bays H. Adiposopathy, metabolic syndrome, quantum physics, general relativity, chaos and the Theory of Everything. Expet Rev Cardiovasc Ther 2005;3:393–404.
[91] Feinman RD, Fine EJ. A calorie is a calorie" violates the second law of thermodynamics. Nutr J 2004;3:9.
[92] Kostic MM. The second law and entropy misconceptions demystified. Entropy 2020;22.
[93] Riedl RA, Burnett CML, Pearson NA, Reho JJ, Mokadem M, Edwards RA, et al. Gut Microbiota Represent a Major Thermogenic Biomass. Function. 2021;2.
[94] Bo S, Fadda M, Fedele D, Pellegrini M, Ghigo E, Pellegrini N. A critical review on the role of food and nutrition in the energy balance. Nutrients 2020;12.
[95] Quatela A, Callister R, Patterson A, MacDonald-Wicks L. The energy content and composition of meals consumed after an overnight fast and their effects on diet induced thermogenesis: a systematic review, meta-analyses and meta-regressions. Nutrients 2016;8:670.
[96] Riggs AJ, White BD, Gropper SS. Changes in energy expenditure associated with ingestion of high protein, high fat versus high protein, low fat meals among underweight, normal weight, and overweight females. Nutr J 2007;6:40.
[97] Abdullah E, Lee JB, Notay K, Millar PJ. Postprandial superior mesenteric artery blood flow is related to changes in peripheral pulse wave harmonics and heart rate: implications for wearable technology? J Appl Physiol 2021;131:681–8. 1985.
[98] Hall M, Walicka M, Panczyk M, Traczyk I. Metabolic parameters in patients with suspected reactive hypoglycemia. J Personalized Med 2021:11.
[99] Khemani P, Mehdirad AA. Cardiovascular disorders mediated by autonomic nervous system dysfunction. Cardiol Rev 2020;28:65–72.
[100] Zysko D, Jamil RT, Anilkumar AC. Tilt table. StatPearls. Treasure island (FL). StatPearls Publishing; 2022. Copyright © 2022, StatPearls Publishing LLC.
[101] Al Nou'mani J, Al Alawi AM, Falhammar H, Al Qassabi A. Orthostatic intolerance after bariatric surgery: a systematic review and meta-analysis. Clin Obes 2021;11:e12483.
[102] Zhang JB, Tamboli RA, Albaugh VL, Williams DB, Kilkelly DM, Grijalva CG, et al. The incidence of orthostatic intolerance after bariatric surgery. Obes Sci Pract 2020;6:76–83.
[103] Schiavon CA, Bersch-Ferreira AC, Santucci EV, Oliveira JD, Torreglosa CR, Bueno PT, et al. Effects of bariatric surgery in obese patients with hypertension: the GATEWAY randomized trial (gastric bypass to treat obese patients with steady hypertension). Circulation 2018;137:1132–42.
[104] Calcagno M, Kahleova H, Alwarith J, Burgess NN, Flores RA, Busta ML, et al. The thermic effect of food: a review. J Am Coll Nutr 2019;38:547–51.
[105] Stob NR, Bell C, MAv Baak, Seals DR. Thermic effect of food and β-adrenergic thermogenic responsiveness in habitually exercising and sedentary healthy adult humans. J Appl Physiol 2007;103:616–22.
[106] Denzer CM, Young JC. The effect of resistance exercise on the thermic effect of food. Int J Sport Nutr Exerc Metabol 2003;13:396–402.

[107] Romon M, Edme JL, Boulenguez C, Lescroart JL, Frimat P. Circadian variation of diet-induced thermogenesis. Am J Clin Nutr 1993;57:476–80.
[108] Richter J, Herzog N, Janka S, Baumann T, Kistenmacher A, Oltmanns KM. Twice as high diet-induced thermogenesis after breakfast vs dinner on high-calorie as well as low-calorie meals. J Clin Endocrinol Metab 2020:105.
[109] Granata GP, Brandon LJ. The thermic effect of food and obesity: discrepant results and methodological variations. Nutr Rev 2002;60:223–33.
[110] Watanabe T, Nomura M, Nakayasu K, Kawano T, Ito S, Nakaya Y. Relationships between thermic effect of food, insulin resistance and autonomic nervous activity. J Med Invest 2006;53:153–8.
[111] Ravussin E, Acheson KJ, Vernet O, Danforth E, Jéquier E. Evidence that insulin resistance is responsible for the decreased thermic effect of glucose in human obesity. J Clin Investigation 1985;76:1268–73.
[112] Gibson AA, Seimon RV, Lee CM, Ayre J, Franklin J, Markovic TP, et al. Do ketogenic diets really suppress appetite? A systematic review and meta-analysis. Obes Rev : Off J Int Assoc Study Obesity 2015;16:64–76.
[113] Vega-López S, Venn BJ, Slavin JL. Relevance of the glycemic index and glycemic load for body weight, diabetes, and cardiovascular disease. Nutrients 2018;10.
[114] Gaesser GA, Miller Jones J, Angadi SS. Perspective: does glycemic index matter for weight loss and obesity prevention? Examination of the evidence on "fast" compared with "slow" carbs. Adv Nutr 2021;12:2076–84.
[115] Dwivedi AK, Dubey P, Reddy SY, Clegg DJ. Associations of glycemic index and glycemic load with cardiovascular disease: updated evidence from meta-analysis and cohort studies. Curr Cardiol Rep 2022;24:141–61.
[116] Sievenpiper JL. Low-carbohydrate diets and cardiometabolic health: the importance of carbohydrate quality over quantity. Nutr Rev 2020;78:69–77.
[117] Wei J, Heng W, Gao J. Effects of low glycemic index diets on gestational diabetes mellitus: a meta-analysis of randomized controlled clinical trials. Medicine (Baltim) 2016;95:e3792.
[118] Salari-Moghaddam A, Keshteli AH, Haghighatdoost F, Esmaillzadeh A, Adibi P. Dietary glycemic index and glycemic load in relation to general obesity and central adiposity among adults. Clinical Nutr 2019;38:2936–42.
[119] Bays HE, Shrestha A, Niranjan V, Khanna M, Kambhamettu L. Obesity pillars roundtable: obesity and South Asians. Obesity Pillars 2022;1:100006.
[120] Reutrakul S, Van Cauter E. Sleep influences on obesity, insulin resistance, and risk of type 2 diabetes. Metab Clin Exp 2018;84:56–66.
[121] Bays HE. Evaluation and practical management of increased visceral fat: should cardiologists lose sleep over it? J Am Coll Cardiol 2022. https://doi.org/10.1016/j.jacc.2022.01.039. IN PRESS.
[122] Shechter A, Rising R, Wolfe S, Albu JB, St-Onge MP. Postprandial thermogenesis and substrate oxidation are unaffected by sleep restriction. Int J Obes 2014;38:1153–8.
[123] Hall KD, Ayuketah A, Brychta R, Cai H, Cassimatis T, Chen KY, et al. Ultra-processed diets cause excess calorie intake and weight gain: an inpatient randomized controlled trial of ad libitum food intake. Cell Metabol 2019;30:226.
[124] Monteiro CA, Cannon G, Moubarac JC, Levy RB, Louzada MLC, Jaime PC. The UN Decade of Nutrition, the NOVA food classification and the trouble with ultra-processing. Publ Health Nutr 2018;21:5–17.
[125] Monteiro CA, Cannon G, Levy RB, Moubarac JC, Louzada ML, Rauber F, et al. Ultra-processed foods: what they are and how to identify them. Publ Health Nutr 2019;22:936–41.
[126] Gorzynik-Debicka M, Przychodzen P, Cappello F, Kuban-Jankowska A, Marino Gammazza A, Knap N, et al. Potential health benefits of olive oil and plant polyphenols. Int J Mol Sci 2018;19.
[127] Rico-Campa A, Martinez-Gonzalez MA, Alvarez-Alvarez I, Mendonca RD, de la Fuente-Arrillaga C, Gomez-Donoso C, et al. Association between consumption of ultra-processed foods and all cause mortality: SUN prospective cohort study. Bmj 2019;365:l1949.
[128] Srour B, Fezeu LK, Kesse-Guyot E, Alles B, Mejean C, Andrianasolo RM, et al. Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Sante). Bmj 2019;365:l1451.
[129] Vandevijvere S, Jaacks LM, Monteiro CA, Moubarac JC, Girling-Butcher M, Lee AC, et al. Global trends in ultraprocessed food and drink product sales and their association with adult body mass index trajectories. Obes Rev : Off J Int Assoc Study Obesity 2019.
[130] Ludwig DS, Astrup A, Bazzano LA, Ebbeling CB, Heymsfield SB, King JC, et al. Ultra-processed food and obesity: the pitfalls of extrapolation from short studies. Cell Metabol 2019;30:3–4.
[131] Gibney MJ, Forde CG, Mullally D, Gibney ER. Ultra-processed foods in human health: a critical appraisal. Am J Clin Nutr 2017;106:717–24.
[132] Elizabeth L, Machado P, Zinöcker M, Baker P, Lawrence M. Ultra-processed foods and health outcomes: a narrative review. Nutrients 2020;12.
[133] Gearhardt AN, Schulte EM. Is food addictive? A review of the science. Annu Rev Nutr 2021;41:387–410.
[134] Betts JA, Chowdhury EA, Gonzalez JT, Richardson JD, Tsintzas K, Thompson D. Is breakfast the most important meal of the day? Proc Nutr Soc 2016;75:464–74.
[135] Ardeshirlarijani E, Namazi N, Jabbari M, Zeinali M, Gerami H, Jalili RB, et al. The link between breakfast skipping and overweigh/obesity in children and adolescents: a meta-analysis of observational studies. J Diabetes Metab Disord 2019;18:657–64.
[136] Li ZH, Xu L, Dai R, Li LJ, Wang HJ. Effects of regular breakfast habits on metabolic and cardiovascular diseases: a protocol for systematic review and meta-analysis. Medicine (Baltim) 2021;100:e27629.
[137] Rong S, Snetselaar LG, Xu G, Sun Y, Liu B, Wallace RB, et al. Association of skipping breakfast with cardiovascular and all-cause mortality. J Am Coll Cardiol 2019;73:2025–32.
[138] Ballon A, Neuenschwander M, Schlesinger S. Breakfast skipping is associated with increased risk of type 2 diabetes among adults: a systematic review and meta-analysis of prospective cohort studies. J Nutr 2019;149:106–13.
[139] Sievert K, Hussain SM, Page MJ, Wang Y, Hughes HJ, Malek M, et al. Effect of breakfast on weight and energy intake: systematic review and meta-analysis of randomised controlled trials. Bmj 2019;364:l42.
[140] Chowdhury EA, Richardson JD, Holman GD, Tsintzas K, Thompson D, Betts JA. The causal role of breakfast in energy balance and health: a randomized controlled trial in obese adults. Am J Clin Nutr 2016;103:747–56.
[141] Dhurandhar EJ. True, true, unrelated? A review of recent evidence for a causal influence of breakfast on obesity. Curr Opin Endocrinol Diabetes Obes 2016;23:384–8.
[142] Ursell LK, Metcalf JL, Parfrey LW, Knight R. Defining the human microbiome. Nutr Rev 2012;70(Suppl 1):S38–44.
[143] Muscogiuri G, Cantone E, Cassarano S, Tuccinardi D, Barrea L, Savastano S, et al. Gut microbiota: a new path to treat obesity. Int J Obes Suppl 2019;9:10–9.
[144] Karczewski J, Zielińska A, Staszewski R, Eder P, Dobrowolska A, Souto EB. Obesity and the brain. Int J Mol Sci 2022;23.
[145] Martínez-Montoro JI, Damas-Fuentes M, Fernández-García JC, Tinahones FJ. Role of the gut microbiome in beta cell and adipose tissue crosstalk: a review. Front Endocrinol 2022;13:869951.
[146] Li D, Li Y, Yang S, Lu J, Jin X, Wu M. Diet-gut microbiota-epigenetics in metabolic diseases: from mechanisms to therapeutics. Biomed Pharmacother 2022;153:113290.
[147] Vallianou N, Dalamaga M, Stratigou T, Karampela I, Tsigalou C. Do antibiotics cause obesity through long-term alterations in the gut microbiome? A review of current evidence. Curr Obes Rep 2021;10:244–62.
[148] Bays HE, Jones PH, Jacobson TA, Cohen DE, Orringer CE, Kothari S, et al. Lipids and bariatric procedures part 1 of 2: scientific statement from the national lipid association, American society for metabolic and bariatric surgery, and obesity medicine association: full report. J Clin lipidol 2016;10:33–57.
[149] Allegretti JR, Kassam Z, Mullish BH, Chiang A, Carrellas M, Hurtado J, et al. Effects of fecal microbiota transplantation with oral capsules in obese patients. Clin Gastroenterol Hepatol : Off Clin Pract J Am Gastroenterol Assoc 2019.
[150] Sehgal K, Khanna S. Gut microbiota: a target for intervention in obesity. Expet Rev Gastroenterol Hepatol 2021;15:1169–79.
[151] Brown AGM, Esposito LE, Fisher RA, Nicastro HL, Tabor DC, Walker JR. Food insecurity and obesity: research gaps, opportunities, and challenges. Translat Behav Med 2019;9:980–7.
[152] Cooksey-Stowers K, Schwartz MB, Brownell KD. Food swamps predict obesity rates better than food deserts in the United States. Int J Environ Res Publ Health 2017;14.
[153] Alcorta A, Porta A, Tárrega A, Alvarez MD, Vaquero MP. Foods for plant-based diets: challenges and innovations. Foods 2021;10.
[154] Kim H, Caulfield LE, Garcia-Larsen V, Steffen LM, Coresh J, Rebholz CM. Plant-based diets are associated with a lower risk of incident cardiovascular disease, cardiovascular disease mortality, and all-cause mortality in a general population of middle-aged adults. J Am Heart Assoc 2019;8:e012865.
[155] Singh PN, Arthur KN, Orlich MJ, James W, Purty A, Job JS, et al. Global epidemiology of obesity, vegetarian dietary patterns, and noncommunicable disease in Asian Indians. Am J Clin Nutr 2014;100(Suppl 1). 359s-64s.
[156] Venkatrao M, Nagarathna R, Majumdar V, Patil SS, Rathi S, Nagendra H. Prevalence of obesity in India and its neurological implications: a multifactor Analysis of a nationwide cross-sectional study. Ann Neurosci 2020;27:153–61.
[157] Borude S. Which is a good diet-veg or non-veg? Faith-based vegetarianism for protection from obesity-a myth or actuality? Obes Surg 2019.
[158] Bays HE, Antoun J, Censani M, Bailony R, Alexander L. Obesity pillars roundtable: obesity and individuals from the Mediterranean region and Middle East. Obesity Pillars 2022;2:100013.
[159] Lisboa PC, Miranda RA, Souza LL, Moura EG. Can breastfeeding affect the rest of our life? Neuropharmacology 2021;200:108821.
[160] Woo JG, Martin LJ. Does breastfeeding protect against childhood obesity? Moving beyond observational evidence. Curr Obes Rep 2015;4:207–16.
[161] Bjerregaard LG, Pedersen DC, Mortensen EL, Sorensen TIA, Baker JL. Breastfeeding duration in infancy and adult risks of type 2 diabetes in a high-income country. Matern Child Nutr 2019:e12869.
[162] Verduci E, Banderali G, Barberi S, Radaelli G, Lops A, Betti F, et al. Epigenetic effects of human breast milk. Nutrients 2014;6:1711–24.
[163] Ventura AK. Does breastfeeding shape food preferences? Links to obesity. Ann Nutr Metab 2017;70(3):8–15.
[164] Meek JY, Noble L, So Breastfeeding. Policy statement: breastfeeding and the use of human milk. Pediatrics 2022:150.
[165] Azad MB, Vehling L, Chan D, Klopp A, Nickel NC, McGavock JM, et al. Infant feeding and weight gain: separating breast milk from breastfeeding and formula from food. Pediatrics 2018;142.
[166] Dewey KG, Güngör D, Donovan SM, Madan EM, Venkatramanan S, Davis TA, et al. Breastfeeding and risk of overweight in childhood and beyond: a systematic review with emphasis on sibling-pair and intervention studies. Am J Clin Nutr 2021;114:1774–90.
[167] Horta BL, Rollins N, Dias MS, Garcez V, Pérez-Escamilla R. Systematic review and meta-analysis of breastfeeding and later overweight or obesity expands on previous study for World Health Organization. Acta Paediatr 2022.
[168] Qiao J, Dai LJ, Zhang Q, Ouyang YQ. A meta-analysis of the association between breastfeeding and early childhood obesity. J Pediatr Nurs 2020;53:57–66.
[169] Sayres S, Visentin L. Breastfeeding: uncovering barriers and offering solutions. Curr Opin Pediatr 2018;30:591–6.

[170] Browne NT, Cuda SE. Nutritional and activity recommendations for the child with normal weight, overweight, and obesity with consideration of food insecurity: an Obesity Medical Association (OMA) Clinical Practice Statement 2022. Obesity Pillars 2022;2:100012.
[171] Lambrinou CP, Karaglani E, Manios Y. Breastfeeding and postpartum weight loss. Curr Opin Clin Nutr Metab Care 2019;22:413–7.
[172] Neville CE, McKinley MC, Holmes VA, Spence D, Woodside JV. The relationship between breastfeeding and postpartum weight change–a systematic review and critical evaluation. Int J Obes 2014;38:577–90.
[173] Jones KM, Power ML, Queenan JT, Schulkin J. Racial and ethnic disparities in breastfeeding. Breastfeed Med 2015;10:186–96.
[174] Jevitt C, Hernandez I, Groër M. Lactation complicated by overweight and obesity: supporting the mother and newborn. J Midwifery Wom Health 2007;52:606–13.
[175] Bardanzellu F, Puddu M, Peroni DG, Fanos V. The human breast milk metabolome in overweight and obese mothers. Front Immunol 2020;11:1533.
[176] Christenson A, Johansson E, Reynisdottir S, Torgerson J, Hemmingsson E. Shame and avoidance as barriers in midwives' communication about body weight with pregnant women: a qualitative interview study. Midwifery 2018;63:1–7.
[177] Pérez-Escamilla R, Buccini GS, Segura-Pérez S, Piwoz E. Perspective: should exclusive breastfeeding still Be recommended for 6 Months? Adv Nutr 2019;10: 931–43.
[178] Dalrymple KV, Flynn AC, Relph SA, O'Keeffe M, Poston L. Lifestyle interventions in overweight and obese pregnant or postpartum women for postpartum weight management: a systematic review of the literature. Nutrients 2018;10.
[179] Scaglioni S, De Cosmi V, Ciappolino V, Parazzini F, Brambilla P, Agostoni C. Factors influencing children's eating behaviours. Nutrients 2018;10.
[180] Xu H, Wen LM, Rissel C. Associations of parental influences with physical activity and screen time among young children: a systematic review. J Obesity 2015;2015: 546925.
[181] Klein S. The case of visceral fat: argument for the defense. J Clin Investigation 2004;113:1530–2.
[182] Bays H. Central obesity as a clinical marker of adiposopathy; increased visceral adiposity as a surrogate marker for global fat dysfunction. Curr Opin Endocrinol Diabetes Obes 2014;21:345–51.
[183] Tomlinson DJ, Erskine RM, Morse CI, Winwood K, Onambélé-Pearson G. The impact of obesity on skeletal muscle strength and structure through adolescence to old age. Biogerontology 2016;17:467–83.
[184] Hoffmans M, Pfeifer WA, Gundlach BL, Nijkrake HG, Oude Ophuis AJ, Hautvast JG. Resting metabolic rate in obese and normal weight women. Int J Obes 1979;3:111–8.
[185] Jéquier E. Energy metabolism in human obesity. Sozial- Präventivmed 1989;34: 58–62.
[186] Ravussin E, Burnand B, Schutz Y, Jéquier E. Twenty-four-hour energy expenditure and resting metabolic rate in obese, moderately obese, and control subjects. Am J Clin Nutr 1982;35:566–73.
[187] Schwartz A, Doucet E. Relative changes in resting energy expenditure during weight loss: a systematic review. Obes Rev : Off J Int Assoc Study Obesity 2010;11: 531–47.
[188] Frankenfield D, Roth-Yousey L, Compher C. Comparison of predictive equations for resting metabolic rate in healthy nonobese and obese adults: a systematic review. J Am Diet Assoc 2005;105:775–89.
[189] Wallhuss A, Isik M, Nystrom FH. Comparison of the subjective sense of high or low metabolism and objectively measured resting metabolic rate. Scand J Clin Lab Invest 2010;70:334–7.
[190] Skov AR, Toubro S, Buemann B, Astrup A. Normal levels of energy expenditure in patients with reported 'low metabolism'. Clin Physiol 1997;17:279–85.
[191] Pettersen AK, Marshall DJ, White CR. Understanding variation in metabolic rate. J Exp Biol 2018;221.
[192] Buscemi S, Verga S, Caimi G, Cerasola G. A low resting metabolic rate is associated with metabolic syndrome. Clinical Nutr 2007;26:806–9.
[193] Anthanont P, Jensen MD. Does basal metabolic rate predict weight gain? Am J Clin Nutr 2016;104:959–63.
[194] Carneiro IP, Elliott SA, Siervo M, Padwal R, Bertoli S, Battezzati A, et al. Is obesity associated with altered energy expenditure? Adv Nutr 2016;7:476–87.
[195] Martin A, Fox D, Murphy CA, Hofmann H, Koehler K. Tissue losses and metabolic adaptations both contribute to the reduction in resting metabolic rate following weight loss. Int J Obes 2022;46:1168–75.
[196] Martins C, Gower BA, Hunter GR. Metabolic adaptation delays time to reach weight loss goals. Obesity 2022;30:400–6.
[197] Hunter GR, Singh H, Carter SJ, Bryan DR, Fisher G. Sarcopenia and its implications for metabolic health. J Obesity 2019;2019:8031705.
[198] Dodds RM, Roberts HC, Cooper C, Sayer AA. The epidemiology of sarcopenia. J Clin Densitom : Off J Int Soc Clin Densitometry 2015;18:461–6.
[199] Rossi AP, Rubele S, Calugi S, Caliari C, Pedelini F, Soave F, et al. Weight cycling as a risk factor for low muscle mass and strength in a population of males and females with obesity. Obesity 2019;27:1068–75.
[200] Ilich JZ, Kelly OJ, Inglis JE. Osteosarcopenic obesity syndrome: what is it and how can it Be identified and diagnosed? Curr Gerontol Geriatr Res 2016;2016: 7325973.
[201] DeMik DE, Marinier MC, Glass NA, Elkins JM. Prevalence of sarcopenia and sarcopenic obesity in an academic total joint arthroplasty practice. Arthroplast Today 2022;16:124–9.
[202] McCarthy D, Berg A. Weight loss strategies and the risk of skeletal muscle mass loss. Nutrients 2021;13.
[203] Cava E, Yeat NC, Mittendorfer B. Preserving healthy muscle during weight loss. Adv Nutr 2017;8:511–9.
[204] Dicker D, Alfadda AA, Coutinho W, Cuevas A, Halford JCG, Hughes CA, et al. Patient motivation to lose weight: importance of healthcare professional support, goals and self-efficacy. Eur J Intern Med 2021;91:10–6.
[205] Trexler ET, Smith-Ryan AE, Norton LE. Metabolic adaptation to weight loss: implications for the athlete. J Int Soc Sports Nutr 2014;11:7.
[206] von Loeffelholz C, Birkenfeld A. The role of non-exercise activity thermogenesis in human obesity. In: Feingold KR, Anawalt B, Boyce A, Chrousos G, de Herder WW, Dungan K, et al., editors. Endotext. South Dartmouth (MA); 2000.
[207] Fehily AM, Butland BK, Yarnell JW. Body fatness and frame size: the Caerphilly study. Eur J Clin Nutr 1990;44:107–11.
[208] Komiya S, Masuda T, Ube M, Mitsuzono R. Body size and composition in different somatotypes of Japanese college-aged women. J Physiol Anthropol 1996;15:5–11.
[209] Katch VL, Freedson PS. Body size and shape: derivation of the "HAT" frame size model. Am J Clin Nutr 1982;36:669–75.
[210] Salamat MR, Salamat AH, Janghorbani M. Association between obesity and bone mineral density by gender and menopausal status. Endocrinol Metab (Seoul) 2016; 31:547–58.
[211] Li Y. Association between obesity and bone mineral density in middle-aged adults. J Orthop Surg Res 2022;17:268.
[212] Jain RK, Vokes T. Fat mass has negative effects on bone, especially in men: a cross-sectional analysis of nhanes 2011-2018. J Clin Endocrinol Metab 2022;107: e2545–52.
[213] Katch VL, Katch FI, Moffatt R, Gittleson M. Muscular development and lean body weight in body builders and weight lifters. Med Sci Sports Exerc 1980;12:340–4.
[214] Silva HG, Mendonca LM, Conceicao FL, Zahar SE, Farias ML. Influence of obesity on bone density in postmenopausal women. Arquivos brasileiros de endocrinologia e metabologia 2007;51:943–9.
[215] Corina M, Vulpoi C, Brănişteanu D. Relationship between bone mineral density, weight, and estrogen levels in pre and postmenopausal women. Rev Med-Chir Soc Med Nat Iasi 2012;116:946–50.
[216] Crepaldi G, Romanato G, Tonin P, Maggi S. Osteoporosis and body composition. J Endocrinol Invest 2007;30:42–7.
[217] Sipilä S, Törmäkangas T, Sillanpää E, Aukee P, Kujala UM, Kovanen V, et al. Muscle and bone mass in middle-aged women: role of menopausal status and physical activity. J Cachexia Sarcopenia Muscle 2020;11:698–709.
[218] Sutter T, Toumi H, Valery A, El Hage R, Pinti A, Lespessailles E. Relationships between muscle mass, strength and regional bone mineral density in young men. PLoS One 2019;14:e0213681.
[219] Barazzoni R, Bischoff S, Boirie Y, Busetto L, Cederholm T, Dicker D, et al. Sarcopenic obesity: time to meet the challenge. Obes Facts 2018;11:294–305.
[220] Clynes MA, Gregson CL, Bruyère O, Cooper C, Dennison EM. Osteosarcopenia: where osteoporosis and sarcopenia collide. Rheumatology 2021;60:529–37.
[221] Chirachariyavej T, Limburanasombat S, Tiensuwan M. The relationship between bone and ash weight to body weight and body length of Thai corpses in Bangkok and central part of Thailand after cremation. J Med Assoc Thai 2007;90:1872–8.
[222] Noakes TD. Hiding unhealthy heart outcomes in a low-fat diet trial: the Women's Health Initiative Randomized Controlled Dietary Modification Trial finds that postmenopausal women with established coronary heart disease were at increased risk of an adverse outcome if they consumed a low-fat 'heart-healthy' diet. Open heart 2021;8.
[223] Fischer NM, Pallazola VA, Xun H, Cainzos-Achirica M, Michos ED. The evolution of the heart-healthy diet for vascular health: a walk through time. Vasc Med 2020; 25:184–93.
[224] Mentella MC, Scaldaferri F, Ricci C, Gasbarrini A, Miggiano GAD. Cancer and mediterranean diet: a review. Nutrients 2019;11.
[225] Meckling KA, O'Sullivan C, Saari D. Comparison of a low-fat diet to a low-carbohydrate diet on weight loss, body composition, and risk factors for diabetes and cardiovascular disease in free-living, overweight men and women. J Clin Endocrinol Metab 2004;89:2717–23.
[226] Leavy JM, Clifton PM, Keogh JB. The role of choice in weight loss strategies: a systematic review and meta-analysis. Nutrients 2018;10.
[227] Borradaile KE, Halpern SD, Wyatt HR, Klein S, Hill JO, Bailer B, et al. Relationship between treatment preference and weight loss in the context of a randomized controlled trial. Obesity 2012;20:1218–22.
[228] Yancy Jr WS, McVay MA, Voils CI. Effect of allowing choice of diet on weight loss–in response. Ann Intern Med 2015;163:805–6.
[229] Melanson EL, Keadle SK, Donnelly JE, Braun B, King NA. Resistance to exercise-induced weight loss: compensatory behavioral adaptations. Med Sci Sports Exerc 2013;45:1600–9.
[230] Ainsworth BE. Compendium of physical activities. Med Sci Sports Exerc 2011;43: 1575. 2011.
[231] Thomas DM, Gonzalez MC, Pereira AZ, Redman LM, Heymsfield SB. Time to correctly predict the amount of weight loss with dieting. J Acad Nutr Diet 2014; 114:857–61.
[232] Murray B, Rosenbloom C. Fundamentals of glycogen metabolism for coaches and athletes. Nutr Rev 2018;76:243–59.
[233] Hall KD, Chen KY, Guo J, Lam YY, Leibel RL, Mayer LE, et al. Energy expenditure and body composition changes after an isocaloric ketogenic diet in overweight and obese men. Am J Clin Nutr 2016;104:324–33.
[234] Zamora Navarro S, Pérez-Llamas F. Errors and myths in feeding and nutrition: impact on the problems of obesity. Nutr Hosp 2013;28(Suppl 5):81–8.
[235] Cole J. Assessing the calorific significance of episodes of human cannibalism in the Palaeolithic. Sci Rep 2017;7:44707.
[236] Franz MJ, VanWormer JJ, Crain AL, Boucher JL, Histon T, Caplan W, 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;107:1755–67.

[237] Foright RM, Presby DM, Sherk VD, Kahn D, Checkley LA, Giles ED, et al. Is regular exercise an effective strategy for weight loss maintenance? Physiol Behav 2018; 188:86–93.
[238] Wang Z, Ying Z, Bosy-Westphal A, Zhang J, Schautz B, Later W, et al. Specific metabolic rates of major organs and tissues across adulthood: evaluation by mechanistic model of resting energy expenditure. Am J Clin Nutr 2010;92: 1369–77.
[239] Sperandei S, Vieira MC, Reis AC. Adherence to physical activity in an unsupervised setting: explanatory variables for high attrition rates among fitness center members. J Sci Med Sport 2016;19:916–20.
[240] Jakicic JM, Davis KK, Rogers RJ, King WC, Marcus MD, Helsel D, et al. Effect of wearable technology combined with a lifestyle intervention on long-term weight loss: the IDEA randomized clinical trial. JAMA, J Am Med Assoc 2016;316: 1161–71.
[241] Sniehotta FF, Evans EH, Sainsbury K, Adamson A, Batterham A, Becker F, et al. Behavioural intervention for weight loss maintenance versus standard weight advice in adults with obesity: a randomised controlled trial in the UK (NULevel Trial). PLoS Med 2019;16:e1002793.
[242] Kononova A, Li L, Kamp K, Bowen M, Rikard RV, Cotten S, et al. The use of wearable activity trackers among older adults: focus group study of tracker perceptions, motivators, and barriers in the maintenance stage of behavior change. JMIR Mhealth Uhealth 2019;7:e9832.
[243] Cheatham SW, Stull KR, Fantigrassi M, Motel I. The efficacy of wearable activity tracking technology as part of a weight loss program: a systematic review. J Sports Med Phys Fit 2018;58:534–48.
[244] Wang W, Cheng J, Song W, Shen Y. The effectiveness of wearable devices as physical activity interventions for preventing and treating obesity in children and adolescents: systematic review and meta-analysis. JMIR Mhealth Uhealth 2022;10: e32435.
[245] Yen HY, Chiu HL. The effectiveness of wearable technologies as physical activity interventions in weight control: a systematic review and meta-analysis of randomized controlled trials. Obes Rev : Off J Int Assoc Study Obesity 2019;20: 1485–93.
[246] McDonough DJ, Su X, Gao Z. Health wearable devices for weight and BMI reduction in individuals with overweight/obesity and chronic comorbidities: systematic review and network meta-analysis. Br J Sports Med 2021;55:917–25.
[247] Wong SH, Tan ZYA, Cheng LJ, Lau ST. Wearable technology-delivered lifestyle intervention amongst adults with overweight and obese: a systematic review and meta-regression. Int J Nurs Stud 2022;127:104163.
[248] Linde JA, Jeffery RW, Levy RL, Pronk NP, Boyle RG. Weight loss goals and treatment outcomes among overweight men and women enrolled in a weight loss trial. Int J Obes 2005;29:1002–5.
[249] Avery A, Langley-Evans SC, Harrington M, Swift JA. Setting targets leads to greater long-term weight losses and 'unrealistic' targets increase the effect in a large community-based commercial weight management group. J Hum Nutr Diet 2016;29:687–96.
[250] Gordon ML, Althoff T, Leskovec J. Goal-setting and achievement in activity tracking apps: a case study of MyFitnessPal. Proc Int World Wide Web Conf 2019; 2019:571–82.
[251] Aaseth J, Ellefsen S, Alehagen U, Sundfør TM, Alexander J. Diets and drugs for weight loss and health in obesity - an update. Biomed Pharmacother 2021;140: 111789.
[252] Rhee EJ. Weight cycling and its cardiometabolic impact. J Obes Metab Syndr 2017;26:237–42.
[253] Di Germanio C, Di Francesco A, Bernier M, de Cabo R. Yo-yo dieting is better than none. Obesity 2018;26:1673.
[254] Dulloo AG, Montani JP. Pathways from dieting to weight regain, to obesity and to the metabolic syndrome: an overview. Obes Rev : Off J Int Assoc Study Obesity 2015;16(Suppl 1):1–6.
[255] Maclean PS, Bergouignan A, Cornier MA, Jackman MR. Biology's response to dieting: the impetus for weight regain. Am J Physiol Regul Integr Comp Physiol 2011;301:R581–600.
[256] Kabiri M, Sexton Ward A, Ramasamy A, van Eijndhoven E, Ganguly R, Smolarz BG, et al. The societal value of broader access to antiobesity medications. Obesity 2020;28:429–36.
[257] Gasoyan H, Tajeu G, Halpern MT, Sarwer DB. Reasons for underutilization of bariatric surgery: the role of insurance benefit design. Surgery for obesity and related diseases. Off J Am Soc Bariatr Surg 2019;15:146–51.
[258] Graham R, Mancher M, Miller Wolman D, Greenfield S, Steinberg E. Clinical practice guidelines we can trust. Washington (DC): National Academies Press; 2011.