ACCSCIENCE PUBLISHING

Global Translational Medicine

PERSPECTIVE ARTICLE

Chronic positive mass balance is the actual etiology of obesity: A living review

Anssi H. Manninen*

Research and Development, Dominus Nutrition Oy, Raahe, Finland

Abstract

The fundamental cause of obesity is widely assumed to be an energy imbalance between calories consumed and calories expended (i.e., the energy balance theory). However, this century-old obesity paradigm is fallacious. According to known laws of physics, the actual etiology of obesity is chronic positive mass balance, not positive energy balance. Furthermore, the relevant physical law in body mass regulation is the Law of Conservation of Mass, not the Law of Conservation of Energy. It is important to understand that energy balance and mass balance are separate balances in the human body. Since calories simply represent the heat released on food oxidation, they have no impact on body mass. Body mass can only change as a result of net mass flow; thus, the only food property that can augment body mass is its nutrient mass, not its energy content. The recently proposed mass balance model describes the temporal evolution of body weight and body composition under a wide variety of feeding experiments, and it seems to provide a highly accurate description of the very best experimental human feeding data. By shifting to a mass balance paradigm of obesity, a deeper understanding of this condition may follow in the near future. The purpose of this living review is to present the core issues of the upcoming paradigm shift and some practical applications related to the subject.

Keywords: Obesity; Body weight regulation; Macronutrients; Energy balance theory; Mass balance model; Paradigm shift; Living review

***Corresponding author:**
Anssi H. Manninen
(anssi@dominusnutrition.fi)

Citation: Manninen AH, 2023, Chronic positive mass balance is the actual etiology of obesity: A living review. *Global Transl Med,* 2(1): 222. https://doi.org/10.36922/gtm.222

Received: October 14, 2022
Accepted: January 26, 2023
Published Online: March 1, 2023

1. Introduction

In the *Twilight of the Idols, or, How to Philosophize with a Hammer*, Friedrich Nietzsche emphasized the significance of "sounding out idols," which entails disclosing the inconsistencies in established metaphysical principles, and "philosophizing with a hammer," a metaphor for the process of critical thinking and questioning to destroy illusions, false beliefs, and prejudices that have become ingrained in people's minds.

Reasoning by analogy refers to building knowledge based on prior assumptions and widely accepted paradigms approved by the majority of people, while reasoning from first principles refers to the practice of actively questioning every assumption one thinks he/she "knows" about a given topic and then creating completely new knowledge from scratch. In other words, reasoning from first principles is the act of boiling a process down to the fundamental parts that one believes are true and building up from there. This approach has been used by many great thinkers, including the ancient philosopher Aristotle. With regard to the present time, no one has utilized reasoning from first

principles as effectively as the world's most successful entrepreneur, Elon Musk.

If we start applying this approach to the regulation of body mass, the first question is what body mass consists of. Almost all of the mass of the human body is made up of four elements: Oxygen (65%), carbon (18.5%), hydrogen (10%), and nitrogen (3.2%). It is essential to note that there are no calories or joules listed. Naturally, the next question would be why obesity researchers pay attention only to energy balance given that energy has no mass at all. Even this short reasoning from first principles reveals that mass balance is more relevant than energy balance.

Recently, Arencibia-Albite has published an exceptionally clever article titled "The energy balance theory (EBT) is an inconsistent paradigm" in the *Journal of Theoretical Biology*[1]. This present article deals with the exact same topic but focuses on practical applications. The purpose is to explain in plain language what this far-reaching paradigm shift will mean on a practical level. Therefore, there will be no complex equations or formulas in this article; instead, the core issues are presented in such a way that every university-educated healthcare professional or scientist can understand them.

Due to the growing interest of the scientific community in the impending paradigm shift, this article has taken up a different approach[2]. As a living review, this article will be updated when new and important information appears.

2. The EBT is a flawed paradigm

It is widely assumed that the fundamental cause of obesity is an energy imbalance between calories consumed and calories expended (i.e., the EBT: "Calories In, Calories Out"). However, according to known laws of physics, this century-old obesity paradigm must be fallacious. The relevant physical law in body mass regulation is the Law of Conservation of Mass, not the Law of Conservation of Energy (*i.e.*, the First Law of Thermodynamics).

This is not a matter of opinion; rather, it is based on exact natural sciences. If matter (mass) can be exchanged between system and surroundings, then the system is an open one. Therefore, all living organisms are open systems, and such systems can be at mass balance even while the system experiences a persistent energy imbalance. That is to say that while energy balance may be positive ($\Delta E > 0$) or negative ($\Delta E < 0$), the Law of Conservation of Energy does not require the mass change that may occur during energy flux to match the energy balance direction[1]. In practice, this means that an energy imbalance does not always lead to a change in body mass. The latter only occurs when one is in a mass imbalance. Body mass decreases in negative mass balance and increases in positive mass balance[1,3].

Since there are widespread misconceptions about thermodynamics and body mass regulation, a brief recap follows.

An open system is a type of thermodynamic system where energy and mass can be exchanged with its surroundings. Consequently, the mass of the system will vary with time. An example is the human body. A closed system, on the other hand, is a type of thermodynamic system where only energy can be exchanged with its surroundings. Consequently, the mass of the system is constant. An example is the refrigerator.

The EBT falsely assumes that there is no difference between the two thermodynamic systems. Contrary to what is almost universally claimed, the EBT is not a consequence of the First Law of Thermodynamics. The claim that the EBT should be valid because of this law is simply not true. Since this is an extremely stubborn misconception, in even plainer English, this type of textbook argument is fallacious:

> *Due to the first law of thermodynamics, a person gains weight when his/her energy intake is greater than his/her energy expenditure.*

Perhaps, it would be more reasonable to say that the statement is partially correct because energy and mass are closely related. Textbooks, however, should read as follows:

> *Due to the Law of Conservation of Mass, a person gains weight when his/her mass intake is greater than his/her mass expenditure.*

3. Law of Conservation of Mass

The Law of Conservation of Mass states that mass can neither be created nor destroyed by chemical or physical changes. In other words, total mass is always conserved. This law dates from Antoine Lavoisier's 1789 discovery par excellence that mass is neither created nor destroyed in any chemical reaction[4]. A clever Frenchman heated mercuric oxide (HgO) and demonstrated that the amount the chemical's mass decreased was equal to the mass of oxygen gas released in the chemical reaction. Lavoisier has proven that mass is conserved in chemical reactions, meaning that the total amount of mass on each side of a chemical equation is always the same. This indicates that the total number of atoms in the reactants must equal the amount in the products regardless of the nature of the chemical change. This forms the basis of stoichiometry, that is, the accounting process by which chemical reactions and equations are mathematically balanced in terms of both mass and number of atoms on each side.

As an example, the oxidation of one generic triglyceride molecule is as follows:

$C_{55}H_{104}O + 78O_2 \rightarrow 55CO_2 + 52H_2O$ + HEAT 8,084 kcal

Reactants		Products	
$C_{55}H_{104}O$	860 g	$55CO_2$	2,420 g
$+78O_2$	2,496 g	$+ 52H_2O$	936 g
	3,356 g		3,356 g

It is important to note that there is mass only in reactants and products but not in energy (calories).

4. Mass-energy equivalence principle

The mass-energy equivalence principle implies that when energy is lost in chemical reactions, the system will also lose a corresponding amount of mass. However, as far as the regulation of body mass is concerned, this equivalence principle has been misunderstood. This global misconception requires detailed clarification.

How is energy intake and expenditure not the governing factors that determine if the body stores the food we eat as fat or not? How could one change that? How can the mass of food change that? If the eventual weight loss is from water, urea, or something else, it is still determined by whether or not the body replaces it or even stores more than was used. Where is the gap where energy expenditure is not representative of the substrate (*i.e.*, mass) being used?

To understand why nutrient mass, not nutritional energy, is the entity that determines body mass fluctuations, one must think in terms of arithmetic and analytical chemistry as shown in the next subsections. The caloric values of macronutrients are rounded.

4.1. Weight gain is the result of mass accumulation, not energy accumulation

Consider two individuals that gained 1 kg of non-water body mass, as they accumulate 1,000 g of absorbed macronutrients within their body cells. The macronutrient distribution of the first subject is shown below.

(i) 200 g of protein = 200 g × 4 kcal/g = 800 kcal
(ii) 300 g of carbohydrate = 300 g × 4 kcal/g = 1,200 kcal
(iii) 500 g of fat = 500 g × 9 kcal/g = 4,500 kcal

The total stored nutritional energy is 800 kcal + 1,200 kcal + 4,500 kcal = 6,500 kcal.

The macronutrient distribution of the second subject is shown below.

(i) 400 g of protein = 400 g × 4 kcal/g = 1,600 kcal
(ii) 400 g of carbohydrate = 400 g × 4 kcal/g = 1,600 kcal
(iii) 200 g of fat = 200g × 9 kcal/g = 1,800 kcal

The total stored nutritional energy is 1,600 kcal + 1,600 kcal + 1,800 kcal = 5,000 kcal.

This example illustrates, therefore, that the property of food that is related to mass gain is its mass, not energy. The first subject, in effect, has accumulated substantially more nutritional energy than the second subject, yet both have experienced the same degree of weight gain.

4.2. Weight loss is the result of mass elimination, not energy expenditure

Consider the oxidation of 100 g of glucose:

$C_6H_{12}O_6 + 6O_2 \rightarrow 6H_2O + 6CO_2$ + HEAT (720 kcal/mol of $C_6H_{12}O_6$)

This requires the uptake of 107 g of oxygen (O_2) as 100 g glucose ($C_6H_{12}O_6$) × (192 g O_2/180 g $C_6H_{12}O_6$) ≈ 107 g O_2. The Law of Conservation of Mass implies that the mass of the products = mass of the reactants. The amount of water (H_2O) and carbon dioxide (CO_2) formed is 207 g as the mass of the products = mass of the reactants = 100 g $C_6H_{12}O_6$ + 107 g O_2 = 207 g.

Now, assume that all the produced water and carbon dioxide are used in the following way:

(i) Water becomes intracellular water in newborn cells;
(ii) Hydrolysis reaction (*i.e.*, the cleavage of a chemical bond by adding a water molecule that becomes part of the reaction products); for example, the release of thyroid hormones thyroxine (T4) and triiodothyronine (T3) requires hydrolysis;
(iii) Carboxylation reaction (*i.e.*, the addition of carbon dioxide to a molecule); for example, carboxylation of acetyl-CoA during fatty acid synthesis.

Notice that in the aforementioned situation, 400 kcal have been expended by oxidizing 100 g of glucose, yet body mass will not decrease when heat is dissipated but rather when the 207 g of reaction products are eliminated, which in the described case did not since, as illustrated, oxidation products become part of the body mass.

The important message in this section is that that energy balance and mass balance are separate balances in the human body[1,3]. This fact should be kept in mind when reading the sections below.

5. Energy balance cannot occur at body mass stability

According to the Law of Conservation of Mass, body mass stability (*i.e.*, mass balance) can occur only when the mean absorbed mass of each macronutrient is the same as its respective mean oxidized mass. Otherwise, body mass will

increase (*i.e.*, absorbed mass > oxidized mass) or decrease (*i.e.*, absorbed mass < oxidized mass).

More specifically, energy balance can occur at body mass stability only if the following three conditions are simultaneously satisfied:

(i) Average absorbed fat mass = Average oxidized fat mass;
(ii) Average absorbed carbohydrate mass = Average oxidized carbohydrate mass;
(iii) Average absorbed protein mass = Average oxidized protein mass.

Clearly, this can never happen. If, for example, all the absorbed protein mass (amino acids) is oxidized, where would the body get building blocks? Therefore, energy balance is unattainable at body mass stability[1,3]. This fact refutes the core idea of the EBT, that is, body mass remains constant in energy balance.

To explain clearly, this section highlights that the following textbook argument is fallacious:

> *When a person is in energy balance, his/her weight stays the same.*

On the contrary, textbooks should read the following:

> *When a person is in energy balance, his/her weight does not stay the same. Since this concept can be difficult to understand, more attention should be paid to the matter. However, the energy balance theory should be also understood since it is important to know what has been known before so that one can quickly grasp new information.*

6. Regulation of body mass

At this point, it should be clear that the regulation of body mass is entirely about detailed mass balances ("Mass In, Mass Out") rather than energy conservation ("Calories In, Calories Out"). The Law of Conservation of Mass guarantees that (i) the O_2 mass that enters cellular respiration plus (ii) the mass of macronutrients that served as energy fuel must be equal to the mass of the excreted oxidation products. This is not a matter of opinion. Daily weight loss must, therefore, be the result of the daily elimination of oxidation products (CO_2, water, urea, sulfur trioxide [SO_3; "Mass Out") rather than a consequence of the heat release upon nutrient combustion (*i.e.*, daily energy expenditure)[5]. It is macronutrient mass intake ("Mass In") that augments body mass; as dictated by the Law of Conservation of Mass, the absorption of 1 g of glucose, protein, or fat increases body mass by exactly 1 g, independent of the substrate's calories. The absorbed nutrient mass cannot be destroyed, and thus will contribute to the total body mass as long as it remains within the body. Such a contribution ends, however, when the nutrients are eliminated from the body either as products of metabolic oxidation or in other forms (*e.g.*, shedding of dead skin cells).

Animals, including humans, ingest food to obtain energy and mass. While energy refers to the capacity to do work, mass is used to build all bodily structures. Not a single gram of body mass is added through energy intake. Since calories represent the heat release upon food oxidation, they have no impact on body mass[1,3]. The term "calorie" comes from the Latin term *calor* (heat). Calorie is broadly defined as the amount of energy needed to increase the temperature of 1 g of water by 1°C. Heat certainly does not produce mass.

The protons and neutrons (*i.e.*, nucleons) that make up an atom account for nearly all of its mass; nuclei contain >99.9% of the mass of an atom. Countless chemical reactions constantly take place in the human body, and energy is bound or released in them. In all these reactions, only electron clouds undergo changes. Atomic nuclei, therefore, always remain intact; changes to the nuclei only occur during nuclear reactions. Body mass can only change as a result of net mass flow[1,3,6]; thus, the only food property that can augment body mass is its nutrient mass, not its energy content (*i.e.*, calories). Like gravity, this is by no means a matter of opinion.

It inevitably follows that any anti-obesity intervention must decrease the intake of energy-providing mass, increase the elimination of oxidation products, or both.

(i) Decrease intake of energy-providing mass (EPM) ("Mass In"), that is, satiating effect. EPM refers to the daily intake of carbohydrate, fat, protein, soluble fiber, and alcohol.
(ii) Increase elimination of oxidation products ("Mass Out"). Each day, we experience weight loss (*i.e.*, body mass loss) given by the weight of energy expenditure-dependent mass loss (EEDML) plus the weight of energy expenditure-independent mass loss (EEIML)[3]. EEDML refers to the daily excretion of EPM oxidation byproducts (CO_2, water, urea, and SO_3), whereas EEIML represents the daily weight loss resulting from (a) the daily elimination of non-metabolically produced water; (b) minerals lost in sweat and urine; (c) fecal matter elimination; and (d) the mass loss from renewal of skin, hair, and nails[3].

A recently proposed mass balance model (MBM)[3] describes the temporal evolution of body weight and body composition under a wide variety of feeding experiments, and it seems to provide a highly accurate description of the very best experimental human feeding data[1,3,7,8]. For example, head-to-head comparisons of the predictions by

the MBM with the EBT-based model of Hall *et al.*[9] have demonstrated that the MBM seems to be superior to the EBT-based model[7]. The difference in prediction accuracy is especially clear when the distribution of macronutrient intake changes drastically, for example, a low-carbohydrate diet versus an isocaloric high-carbohydrate diet. The ranking of such models is determined by their predictive accuracy, which is also the reason for such models to be developed. Emphasizing that the MBM predicts not only the change in total body mass, but also the change in fat mass is essential.

Figure 1, which is adapted from Arencibia-Albite's and Manninen's study[7], presents a comparative simulation between the EBT-based model[9] and the MBM[3]. All data can be found in the original source[7]; therefore, there is no reason to repeat them here. However, it is difficult to understand what these simulation results mean. Hence, the results are presented here in a simple manner (Figure 1). In the simulations, the free-living feeding trial data of Kong *et al.* were used[10]. Twenty young female subjects followed a "normal diet" (ND; carbohydrate 44.0 ± 7.6%, protein 15.4 ± 3.3%, and fat 39.6 ± 5.8%) for 4 weeks as a baseline and then switched to a very-low-carbohydrate/high-fat diet (KD; carbohydrate 9.2 ± 4.8%, protein 21.9 ± 3.4%, and fat 69.0 ± 5.4%) for another 4 weeks. The study showed that the 4-week KD intervention led to marked reductions in body mass (−2.9 kg) and body fat percentage (−2.0%). The results of the MBM-based simulations closely resemble those of the feeding trial, whereas the predictions of the EBT-based simulations are clearly incorrect. It is necessary to pay close attention to how the incorrect formula (Daily Fat Loss) = (Daily Fat Intake) – (Daily Net Fat Oxidation) affects the prediction results of the EBT-based model. The aforementioned formula would be valid only if the net fat oxidation is independent of the diet´s macronutrient distribution. If the net fat oxidation increases as dietary fat intake increases (and *vice versa*), fat loss may be similar among isocaloric diets that vary greatly in fat content. Hall *et al.* respiratory quotient (RQ) data demonstrate that this is indeed the case, as shown in Figure 2C, which indicates that the oxidation of fatty acids increases as the proportion

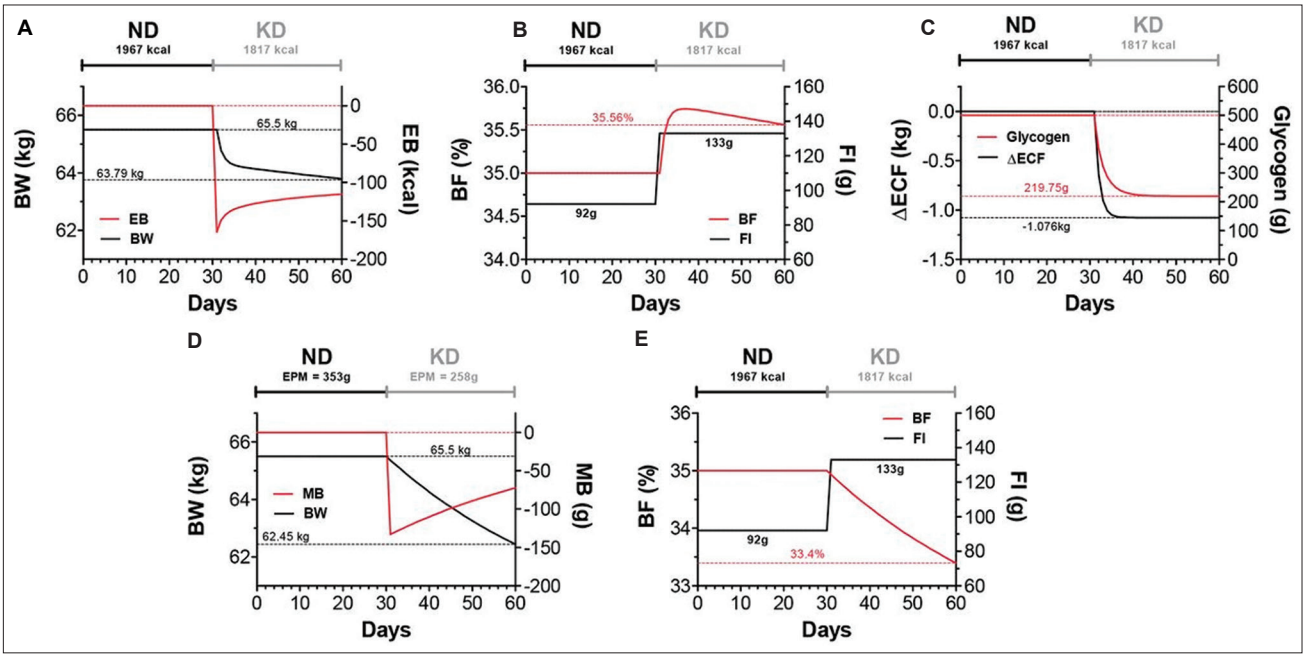

Figure 1. Simulations of Kong *et al.* feeding trial (EBT vs. MBM). (A) During the "normal diet" (ND; days 0–30), the energy balance (EB; red curve) was zero. After day 30, EB became negative following the very-low-carbohydrate/high-fat diet (KD), resulting in a 1.71 kg BW loss at day 60. (B) The EBT-based model by Hall *et al.*[9] predicts that BF percentage increases during the KD although BW decreases. This incorrect prediction was due to the 41 g increase in fat intake (FI) during the KD; the EBT incorrectly assumes that Daily Fat Loss = Daily Fat Intake – Daily Net Fat Oxidation[12]. (C) During the ND, the amount of glycogen stored was 500 g, but during the KD, its amount decreased to 280.25 g; extracellular fluid (ECF) also decreased by 1.076 kg; thus, glycogen + ECF = 1.35625 kg. Of the 1.71 kg weight loss in A, 0.35375 kg (1.71 kg – 1.35625 kg) were from other mass sources: 0.2436 kg fat mass + 0.11015 kg fat-free mass. According to the EBT, this indicates that the total weight loss was distributed as 0.2436 kg of fat mass plus 1.4664 kg of fat-free mass. As the decline in fat-free mass is much larger than that of fat mass, the EBT falsely predicts that the BF percentage will increase as illustrated in B. (D) During the ND period (days 0 – 30), the mass balance (MB; red curve) was zero. After day 30, the MB became negative following the KD, resulting in a 3.05 kg weight loss at day 60. (E) According to the MBM, of the 3.05 kg of weight loss, 2.07 kg came from fat mass and 0.98 kg from fat-free mass. Although the FI increased, the decline in fat-free mass was much smaller than that of fat mass, and thus the BF decreased[7].
BF: Body fat; BW: body weight; EBT: Energy balance theory; MBM: Mass balance model.

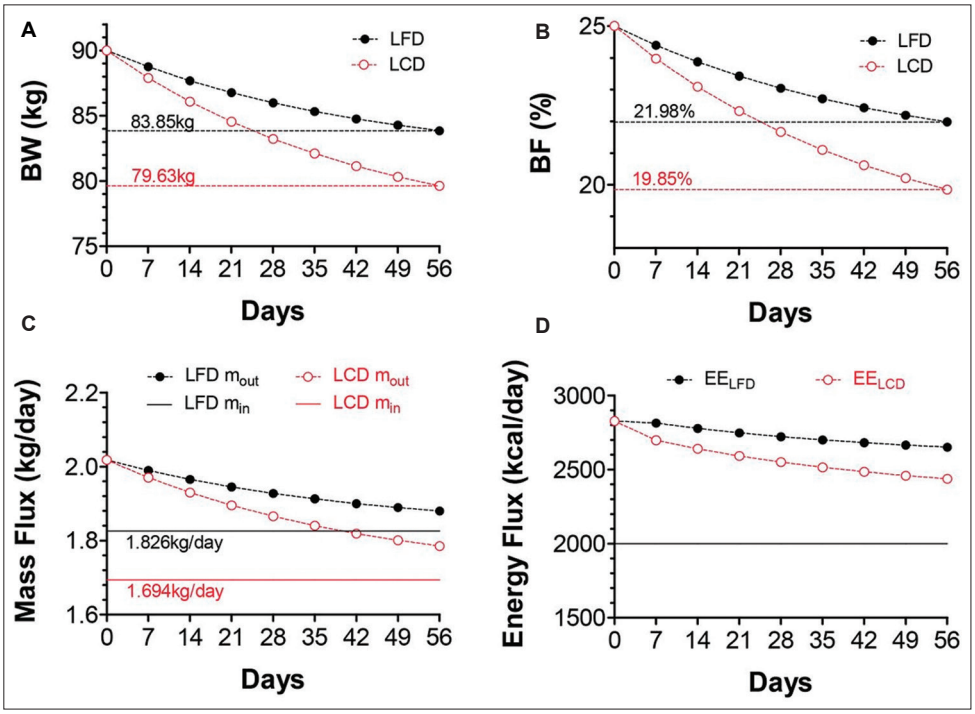

Figure 2. (A-D) Mass balance model (MBM)-based simulation of two hypothetical overweight (90 kg) individuals whose body composition and total energy intake were identical but macronutrient distribution was clearly different. In the initial situation, the nutrient intake was as follows: 2,750 kcal/day; 35% fat (F), 50% carbohydrate (C), and 15% protein (P). These individuals began following either a 2,000 kcal high-carbohydrate/low-fat diet (LFD) or a 2000 kcal low-carbohydrate/high-fat diet (LCD), whose macronutrient distribution was as follows: LFD = 20% F, 65% C, and 15% P; LCD = 70% F, 15% C, and 15% P. According to the energy balance theory, these diets should lead to almost identical effects in terms of body mass and fat mass. However, the MBM predicts that the LCD results in a greater body mass and fat mass loss compared with the LFD. As demonstrated, the nutrient mass intake (m_{in}) was smaller compared with the eliminated mass (m_{out}); thus, the net daily mass loss was larger (*i.e.*, $m_{in} - m_{out}$).
BF: Body fat; BW: body weight.

of fat in the diet increases[11]. For further details, refer to the figure legend.

Although free-living feeding trials are always a mixture of effectiveness and compliance, there is every reason to believe that Kong *et al.* study was a well-controlled study. Several requirements were made to ensure the subjects' adherence to the KD.

(i) All subjects were required to measure their daily urine ketones (early morning or after dinner) and record a 3-day food diary (2 weekdays and 1 week end day) during the experimental period.
(ii) The 3-day food diaries were kept by all subjects for 8 weeks.
(iii) All subjects were given "thorough instructions" on how to estimate portion sizes and record food/beverages intake on food composition tables in advance.
(iv) All subjects were required to report to the laboratory every week to assess changes in body weight and hand-in their logbook with dietary records.
(v) Their energy intake and macronutrient distribution were calculated by the same dietician using the nutrition analysis and management system.
(vi) Their diet compliance was evaluated based on the food diaries and urine ketone results; all subjects received individual follow-up dietary advice and counseling from the dietician.

On the whole, the feeding data produced by Kong *et al.* provide reliable information on the effects of macronutrient distribution on body mass and composition; thus, the simulation comparison would seem to show "beyond reasonable doubt"[13] that the MBM-based simulation provides more accurate predictions than the EBT-based simulation.

As mentioned earlier, Hall *et al.* EBT-based model assumes that body fat fluctuations are the consequence of an imbalance between dietary fat consumption and net fat oxidation. This formula would be valid if the distribution of macronutrients in the diet does not affect the oxidation of fatty acids, but this assumption does not correspond to reality. Hall *et al.* indirectly estimate the reduction in body fat based on the following equations (in g):

Daily Fat Loss = Daily Fat Intake – Daily Net Fat Oxidation (1)

Where Daily Net Fat Oxidation is another estimate calculated by

$$\text{Daily Net Fat Oxidation} = 1.63VO_2 - 1.64VCO_2 - 1.84N \quad (2)$$

Where VO_2 and VCO_2 are the volume (in L) of consumed O_2 and produced CO_2, respectively, while N is the urinary nitrogen excretion per 24 h. In these equations, the only precise numeric input is Daily Fat Intake, whereas Daily Net Fat Oxidation is an estimate obtained from estimates that inevitably increase the inaccuracy of measurement. As recently discussed by Arencibia-Albite[1], the aforementioned equations overlook, among other things, the fact that body fat can also decrease through the excretion of fatty acid derivatives.

7. A low-carbohydrate diet provides less nutrient mass than an isocaloric high-carbohydrate diet

A low-carbohydrate/high-fat diet leads to a greater body mass and fat mass loss than an isocaloric high-carbohydrate/low-fat diet (LFD) because it provides less nutrient mass[1,3,7,8]. When the energy fraction from dietary fat increases, while energy intake is clamped (*i.e.*, fixed), mass intake decreases due to the significantly higher energy density of fat compared with other energy substrates. Such a difference in mass intake translates into greater body mass and fat loss in a low-carbohydrate diet versus an isocaloric high-carbohydrate diet. If such a feeding response is not observed, then it is simply not a well-controlled study, as alternative results would indicate a violation of the Law of Conversation of Mass.

If two persons eliminate body mass at the same daily rate, then the one ingesting less nutrient mass will express a greater daily body mass and fat loss. For instance, the daily energy intake of 2,500 kcal distributed as 30% fat (9.4 kcal/g), 55% carbohydrate (4.2 kcal/g), and 15% protein (4.7 kcal/g) corresponds to a mass intake of ~487 g, whereas the same energy intake distributed as 60% fat, 30% carbohydrate, and 10% protein reduces mass ingestion by ~96 g. This is not a small difference in the long run.

It has been suggested that a low-carbohydrate diet is more effective than an isocaloric high-carbohydrate diet in losing body mass and fat mass because the former lowers insulin levels[14]. However, it is worth noting that insulin or any other hormones cannot create any kind of mass out of thin air. Only ingested nutrient mass can result in increased body mass. Insulin just ensures that this mass can be stored. Similarly, lowered insulin levels cannot magically destroy any mass. Although insulin levels decrease with a low-carbohydrate diet, it is not a causal factor of body mass and fat mass loss. It just happens simultaneously with decreased nutrient mass intake. What about *de novo* lipogenesis (DNL), that is, the process of synthesizing fatty acids from acetyl-CoA subunits? Hyperinsulinemia, caused by the consumption of a large amount of carbohydrates, can increase DNL, but it is only relevant in extreme overfeeding situations. DNL seems to play a central role in the pathogenesis of non-alcoholic fatty liver disease[15] but this topic is beyond the scope of this article.

However, insulin levels can be important in terms of where body fat is reduced. Since high insulin levels favor fat synthesis and inhibit lipolysis, it seems reasonable that the reduction of body fat occurs primarily through a reduction in dietary fat intake during a high-carbohydrate diet. In contrast, a low-carbohydrate diet lowers insulin levels, thus reducing fat synthesis and stimulating lipolysis, which nullify the effects of high dietary fat intake. These factors may explain why low-carbohydrate diets tend to work well for visceral fat reduction[16-18].

Goss *et al.* have recently reported that the very-low-carbohydrate/high-fat diet group in their 8-week study experienced a 3-fold greater loss of visceral adipose tissue (VAT) and intermuscular adipose tissue (IMAT) when compared to the high-carbohydrate/LFD group[17]. Following a very-low-carbohydrate/high-fat diet, there was a significantly greater decrease in fasting insulin level compared to the high-carbohydrate/LFD ($13.7 \pm 5.6 \rightarrow 9.4 \pm 4.0$ vs. $15.6 \pm 6.5 \rightarrow 16.0 \pm 8.2$) μU/mL. It should be noted, however, that the very-low-carbohydrate/high-fat group consumed significantly lesser total calories, and thus nutrient mass, per day than the high-carbohydrate/low-fat group. Nevertheless, it seems that the very-low-carbohydrate/high-fat diet works particularly well on these metabolically harmful fat depots.

Figure 2, which is adapted from Arencibia-Albite's and Manninen's study[7], presents two hypothetical overweight individuals whose body composition and total energy intake were identical but macronutrient distribution was clearly different.

8. A highly controlled metabolic ward feeding trial supporting the mass balance approach

When it comes to proving causality in this matter, metabolic ward studies are considered the gold standard. Unfortunately, the cost of implementing such trials makes it unlikely that any new ones will be conducted in the near future[19]. As of now, the best controlled experiment performed in a metabolic ward is that of Hall *et al.*[11]. The results of the study are in full agreement with the mass

balance approach, and two separate articles by Arencibia-Albite *et al.*[7] and Manninen[12], respectively, have been published on the subject; hence, it will not be discussed further in this present article.

9. Recent meta-analyses of randomized and controlled free-living feeding trials supporting the mass balance approach

Feeding trials performed on free-living subjects are always a mixture of effectiveness and compliance. When subjects are randomized to a certain diet, many are often not very committed to following the prescribed diet. Usually, the macronutrient distribution of the compared diets begins to converge at the latest after 1 year. Nevertheless, a couple of recent meta-analyses on the topic will be reviewed in this paper.

In a meta-analysis by Choi *et al.* eight feeding trials reporting changes in weight-related parameters were included in the study[20]. The results indicated that very-low-carbohydrate/high-fat diets were significantly more effective in reducing body mass than higher carbohydrate control diets; these results are in accordance with the mass balance approach. As aforementioned, when the energy fraction from dietary fat increases, while energy intake is fixed, mass intake decreases due to the significantly higher energy density of fat compared with other energy substrates.

A recent meta-analysis by Zaki *et al.* has compared the effectiveness between very-low-carbohydrate diets and low-carbohydrate diets[21]. In this comparison, the difference in nutrient mass intake was not as significant as in the aforementioned meta-analysis. As can be assumed based on the mass balance approach, those who were on very-low-carbohydrate diets lost slightly more body mass than those on low-carbohydrate diets. There were some variations in the results, which must be attributed to poor compliance.

10. An "old" well-controlled feeding experiment supporting the mass balance approach

In the early seventies, Young *et al.* compared three diets that contained the same amount of calories (1,800 kcal/day) and protein (115 g/day) but different carbohydrate contents[22]. After 9 weeks on the 30-g, 60-g, and 104-g carbohydrate diet, the weight loss was 16.2 kg, 12.8 kg, and 11.9 kg, respectively, and fat accounted for 95%, 84%, and 75% of the weight loss. The authors thus concluded, "Weight loss, fat loss, and percent of weight loss as fat appeared to be inversely related to the level of carbohydrate in the isocaloric, isoprotein diets." This is consistent with the mass balance approach. Since these diligent researchers have followed the EBT paradigm, "no adequate explanation can be given for weight loss differences." Young *et al.* study has not received any substantial criticism. It is worth noting that they utilized underwater weighing (*i.e.*, hydrodensitometry) to determine body composition. This method is more accurate than other widely available methods of body composition testing. When performed properly, underwater weighing may be accurate up to 1.8%–2.8% in comparison with the state-of-the-art methods (*e.g.*, magnetic resonance imaging [MRI] and computed tomography [CT]).

11. Epidemiological data supporting the mass balance approach

As recently pointed out by Mozaffarian[23], the data from the National Health and Nutrition Examination Survey (NHANES) have shown no increase in energy consumption or availability over ≥ 20 years, a time period during which obesity has steadily increased (see Figure 1 in Mozaffarian[23]). In fact, the data from NHANES have suggested a small but statistically significant decline in energy intake over this period[23]. What about the other side of the coin, *i.e.*, energy expenditure? Although there are no similar epidemiological data available on the matter, high-quality studies utilizing the doubly labeled water (DLW) method have indicated that the total energy expenditure (TEE) of Hadza hunter-gatherers was similar to Westerners and other populations in market economies despite their high physical activity level[24]. Therefore, it is clear that the main factor causing the obesity epidemic is increased food intake rather than declined expenditure.

If there has been no change in energy intake and energy consumption, what on earth is causing the obesity epidemic? If we follow the EBT paradigm, this seems paradoxical; however, from the perspective of the mass balance approach, there is nothing surprising about it. According to nutritional recommendations, people should increase their intake of carbohydrates at the expense of fat. If such recommendations are followed, the intake of nutrient mass will increase, while the calorie intake remains the same. The data from NHANES have indicated that the percentage of calories from carbohydrates increased between 1971–1974 and 1999–2000 from 42.4% to 49.0% for men and from 45.4% to 51.6% for women, whereas the percentage of calories from fats decreased from 36.9% to 32.8% for men and from 36.1% to 32.8% for women[25]. Although self-reported dietary intake is subjected to recall bias, there is every reason to assume that strongly marketed nutritional recommendations have produced results in line with the goals at the population level.

In the Women's Health Initiative Observational Study (WHI/OS), the relationship between weight gain and four common diet patterns (a LFD, a reduced-carbohydrate diet, a Mediterranean-style diet, and a diet consistent with the United States Department of Agriculture's [USDA] Dietary Guidelines for Americans [DGA]) was examined[26]. The WHI/OS was a longitudinal study of postmenopausal women aged 49–81 years (n = 93,676) who were enrolled between 1994 and 1998 and followed for up to 8 years. The conclusion made by the researchers states all that is needed: "Our findings therefore challenge prevailing dietary recommendations, suggesting instead that a low-fat (diet) may promote rather than prevent weight gain after menopause." The results were the opposite of what could have been assumed based on the EBT.

12. Extremely obese individuals have very high TEE

Based on the EBT, it has been suggested that low TEE is a risk factor for obesity[27], but the evidence does not support this assumption. The results from the investigation of Das *et al.* on the hypothesis stating that both TEE and resting energy expenditure (REE) are low in extremely obese individuals showed the opposite, wherein the TEE of extremely obese subjects was very high[28]. If the EBT were a valid paradigm, a high TEE should protect against obesity. Similarly, Rimbach *et al.* have concluded, "TEE is not a risk factor for, and high TEE is not protective against, weight or body fat gain over the time intervals tested"[29]. These findings cause more gray hairs for the proponents of the EBT.

13. The timing of nutrient mass ingestion cannot modify the Law of Conservation of Mass

The timing of nutrient mass ingestion will never be able to modify the Law of Conservation of Mass. The timing of nutrient mass ingestion may have an effect on body mass and fat mass only if it affects mass expenditure. A well-controlled feeding trial by Ruddick-Collins *et al.* demonstrates this fact in an excellent manner[30]. They performed a 4-week crossover isocaloric and eucaloric feeding trial, comparing "morning loaded" (45%:35%:20% calories at breakfast: lunch:dinner) versus "evening loaded" (20%:35%:45% calories at breakfast: lunch:dinner) calorie intake. This was a free-living study, but all food and beverages were provided, making it "the most rigorously controlled study to assess timing of eating in humans to date"[30]. As can be assumed based on the mass balance approach, the results indicated no differences in body mass loss, total daily energy expenditure, and resting metabolic rate in relation to the timing of calorie distribution.

14. The results of dietary treatments in the pre-insulin era are in line with the mass balance approach

Some critics of the EBT have rightly pointed out that the results of dietary treatments in the pre-insulin era[31] are not in agreement with this century-old paradigm. In those days, type I diabetics were treated with a diet that was very low in carbohydrate and protein, *that is*, a diet containing mostly fat[31]. The rationality of this was to minimize the excretion of glucose mass in the urine (glucosuria) so that the patient would not starve to death. Protein intake was also kept at low levels since gluconeogenic amino acids can raise blood sugar levels.

The observations of the pre-insulin era in relation to macronutrient distribution and body mass have been simulated. Figure 3, which is adapted from Arencibia-Albite's and Manninen's study[7], shows the results of these simulations.

15. A quick look at a recent article that still tries to defend the EBT

In their recent paper, Hall *et al.*[32] attempted to defend the EBT. They stated, "If we are particularly interested in the storage of energy as body fat, then the energy balance equation $E_{in} - E_{out} = E_{storage}$ can be specified as $E_{in} - E_{out} = E_{fat} + E_{protein} + E_{carbohydrate}$," where E = energy.

With all due respect, these authors do not understand that energy balance and mass balance are separate balances, as has already been discussed. The body stores fat as mass, not as energy, because energy has no mass at all. Moreover, changes in both total body mass and fat mass are due to changes in mass balance.

For the above equation to be valid, the mean absorbed mass of each macronutrient must be equal to its respective mean oxidized mass, which is simply not possible (refer to 5. Energy balance cannot occur at body mass stability).

16. Diet writers' favorite hormones

16.1. Leptin

Leptin, a peptide hormone that is predominantly made by adipose cells, helps to regulate energy balance by inhibiting hunger[33]. According to the EBT, the macronutrient distribution of diet should only have a minimal effect on leptin levels since it has a minimal effect on body mass and fat mass. Hormonal responses have been determined in the aforementioned feeding experiment by Kong *et al.* and their data (Table 1 in Kong *et al.*[10]) have shown the complete opposite of what could be assumed based on the EBT, indicating that switching from a "normal diet"

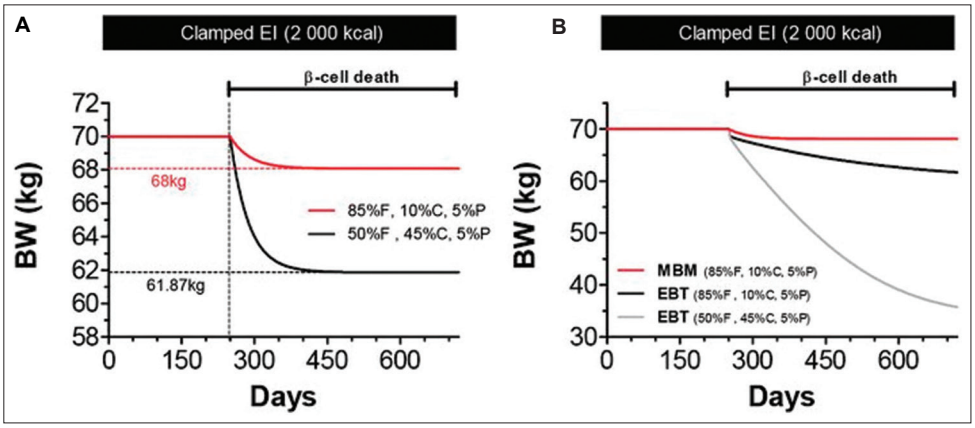

Figure 3. Dietary management of type 1 diabetes: MBM versus EBT simulation. (A) MBM predicts that the reduction in body mass caused by beta-cell death (*i.e.*, onset of diabetes) is highly dependent on the macronutrient distribution of diet, a result that is consistent with the results of dietary treatments in the pre-insulin era[51]. From the source[3], we can see how the model parameters have been modified in these diabetes simulations (*i.e.*, $xC = 0$). (B) The EBT-based model by Hall *et al.*[22] predicts that macronutrient distribution has a significantly lesser effect on body mass reduction.
C: Carbohydrate; BW: Body weight; EBT: Energy balance theory; F: Fat; MBM: Mass balance model; P: Protein.

(carbohydrate 44.0 ± 7.6%, protein 15.4 ± 3.3%, and fat 39.6 ± 5.8%) to a very-low-carbohydrate/high-fat diet (carbohydrate 9.2 ± 4.8%, protein 21.9 ± 3.4%, and fat 69.0 ± 5.4%) can significantly reduce leptin levels. This is consistent with the mass balance approach. The lower the body fat level, the lower the leptin level.

16.2. Insulin (with special reference to the carbohydrate-insulin model)

Insulin, a peptide hormone that is produced by pancreatic beta cells, is considered the main anabolic hormone of the body. This is probably the reason why this hormone has become a favorite of diet writers. The carbohydrate-insulin model (CIM), an obesity-related model, proposes a reversal of causal direction[14]. According to proponents of the CIM, "increasing fat deposition in the body – resulting from the hormonal responses to a high-glycemic-load diet – drives positive energy balance"[14].

It is worth emphasizing that the CIM operates within the EBT; that is, it assumes that a positive energy balance is the cause of obesity. It is, therefore, not a competing paradigm. The direction of causality in this matter does not affect the laws of physics in any way. The physical basis of both the EBT and the CIM operating within it is flawed, as has already been demonstrated.

One of the central claims of the CIM is that high insulin levels promote weight gain, but as already mentioned, insulin cannot create mass from nothing. Although insulin levels decrease with low-carbohydrate diets, it is not a causal factor in body mass and fat mass loss. It just happens simultaneously with decreased nutrient mass intake. Proponents of the CIM suggest that high insulin levels slow down metabolism, thus promoting weight gain[14]; it is worth mentioning that the universal assumption of metabolism being synonymous with energy expenditure is misleading, as metabolism is actually mass expenditure. Ludwig *et al.* have also claimed that their meta-analysis[34] supports this assumption, but the conclusions do not stand up to critical scrutiny[35].

Although, at a cursory glance, it might appear that the CIM is in agreement with the insulin response data, in reality, it is a free passenger traveling on the wing of mass change. The decrease in insulin level and the intake of nutrient mass occurs simultaneously, but only mass can be a causal factor in mass change. In the MBM, it is assumed that the changes in body mass and composition are independent of the physiological effects of a diet. Rather, the differences are due to different amounts of nutrient mass intake. MBM-based simulations provide very convincing evidence for this assumption[1,3,7,8].

As already discussed, however, insulin levels are considered important in terms of where body fat is reduced. In addition, there are other reasons for maintaining low insulin levels. For instance, individuals with hyperinsulinemia are at higher risk of developing obesity, type 2 diabetes, cardiovascular disease, cancer, and premature mortality[36]. It may seem paradoxical at first glance that the statement "insulin cannot create mass" is made, and then an article[36] that lists hyperinsulinemia as a risk factor for obesity is referred to. To clarify the seemingly contradictory matter, it is important to understand that hyperinsulinemia is often caused by the regular consumption of sugar and other refined carbohydrates, while the individual also gains weight. In this situation, insulin does not cause obesity; rather, obesity is caused by a chronic positive mass balance. Here, it is referring to

the etiology, that is, the root cause. According to *Oxford Learner's Dictionaries*, "etiology" refers to "the cause of a disease or medical condition." Although obesity has only one etiology, that is, chronic positive mass balance, it has numerous risk factors, each of which increases, with a certain probability, the occurrence of a positive mass balance; however, none of these risk factors are capable of creating any kind of mass. It is still a matter of balance between intake and expenditure, but in this case, mass balance.

17. Dietary ketosis *per se* does not affect body mass or fat mass

When the rate of mobilization of fatty acids from adipose tissue is accelerated, such as during a very-low-carbohydrate/high-fat ketogenic diet, the liver produces ketone bodies: acetoacetate, beta-hydroxybutyrate, and acetone (a spontaneous breakdown product of acetoacetate). Since the liver cannot utilize ketone bodies, they flow from the liver to extrahepatic tissues (*e.g.*, brain and muscle) for use as fuel.

Although it has been suggested that dietary ketosis could accelerate the reduction of body mass and fat mass, dietary ketosis *per* se does not affect body mass or fat mass if we disregard the scant urine ketone excretion in the initial phase. Mass does not mysteriously disappear. Looking at equation (13) in relation to MBM in Arencibia-Albite[3], it is not necessary to include an extra term for the energy expenditure fraction derived from ketone bodies, as the oxidation of ketone bodies is essentially fat oxidation. For example, the β-oxidation of one palmitic acid molecule yields eight acetyl-coenzyme A molecules, in which two of these react to generate four acetoacetate molecules. Hence, the oxidation of four acetoacetate molecules is equivalent to that of one palmitic acid molecule. For further details, refer to *2.2.1. At energy balance the oxidized macronutrient distribution that results in the* EE_{avg} *is equal to macronutrient distribution in the* EIa_{vg} in Arencibia-Albite[3].

It is impossible to study the matter precisely in a feeding trial setting, as there would be a small difference in the nutrient mass intake between the comparison groups, that is, a very-low-carbohydrate diet group versus an isocaloric low-carbohydrate diet group. More specifically, the nutrient mass intake of the first group is inevitably slightly lower than that of the latter. Remember that when the energy fraction from dietary fat increases, while energy intake is fixed, nutrient mass intake decreases due to the significantly higher energy density of fat compared with other energy substrates. Vidić *et al*. have also investigated the matter and came to a conclusion that a ketogenic diet with sustained hyperketonemia above 1 mol/L has pretty much the same impact on body composition as a low carbohydrate non-ketogenic diet[37].

Dietary ketosis can reduce the feeling of hunger[38], and thereby reduce the intake of nutrient mass; however, this does not undermine the Law of Conservation of Mass.

18. Nutrition facts label

The nutrition facts label on packaged food was updated in 2016 to reflect updated scientific information, including information about the association between diet and chronic diseases, such as obesity and heart disease[39]. One of the most prominent updates of the new food labeling regulations released by the Food and Drug Administration (FDA) is found on the calorie line; the font for calories has been significantly enlarged and emboldened for first-glance reference. This well-intentioned update was based on the rationale that caloric values may be easily comprehended without having to examine the food label in detail. Humans need energy (*i.e.*, the capacity to do work), but calories have no impact on body mass; thus, the calorie line should be replaced or complemented with the mass line (*e.g.*, "Nutrient Mass" or "Mass").

It is also worth noting that the concept of "light product" is misleading. In reality, these products are often "heavy products." When the energy fraction from dietary fat increases, while the energy content remains the same, mass intake decreases due to the significantly higher energy density of fat compared with other energy substrates. A high-carbohydrate "light product" containing 200 kcal provides more mass than a high-fat product containing 200 kcal. This fact should have a significant impact on the prevailing legislation and the operation of the food industry.

In short, dietary fats are therefore not problematic in relation to weight management, as they provide a lot of energy relative to their mass. Dietary fats are only a problem when they are used to make high-carbohydrate food highly palatable. The "light product" concept should be removed from legislation as soon as possible because it misleads consumers in many situations.

19. A flawed paradigm leads to misinterpretation of research data

In research literature, there is plenty of feeding trial reports that seem to support the EBT. A flawed paradigm, however, almost always leads to incorrect interpretations and conclusions. There are many research reports claiming that the more effective weight loss effect of low-carbohydrate diets compared to isocaloric high-carbohydrate diets is attributed to a methodological error (*e.g.*, under-reporting of food consumption and low sensitivity of research

equipment). The assumption is that such results would violate the Law of Conservation of Energy. As has been discussed before, this is not the case (see 2. The energy balance theory is a flawed paradigm). In studies where low-carbohydrate diets have not been more effective in terms of fat loss, EBT-based calculation formulas have been used, which yielded incorrect results (*e.g.*, Hall *et al.*[11] and a reanalysis in Manninen[12]). Therefore, it is important to consider these points when reading such reports.

The real "acid test" of every theory is how good results can be obtained in practice based on the theory. How effective have EBT-based obesity treatment interventions been? As of 2021, 19 US states and territories have at least 35% of their residents living with obesity, which is more than double the number in 2018[40]. Therefore, it is clearly impossible to even talk about effective interventions. Anyone would think that this upsurge would finally raise concerns. However, in my opinion, wasting time and money on research conducted within the EBT paradigm should be stopped immediately.

20. Other applications of the mass balance approach

Although this review focuses on the macronutrient distribution of diet, the mass balance approach has many other practical applications. For example, anti-obesity drugs or dietary supplements that affect satiety should reduce the consumption of carbohydrates instead of fats. Other applications will be covered in the updates to this article.

21. The mass balance approach has nothing to do with the metabolic advantage hypothesis

Contrary to what some have thought, the mass balance approach has nothing to do with the metabolic advantage hypothesis[41]. Proponents of this hypothesis postulate that low-carbohydrate diets lead to faster body mass and fat mass loss than isocaloric high-carbohydrate diets because "energetic inefficiency, substrate cycling, and demands of gluconeogenesis support observed advantages for weight [and fat] loss"[42]. Unlike energy, mass has no efficiency. The amount of mass that is taken in always comes out in exactly the same amount. It is worth noting that the metabolic advantage hypothesis operates within the EBT.

With all due respect, it would seem that the proponents of the metabolic advantage hypothesis have not taken notice that efficiency is not related to incomplete substrate oxidation but to how the body uses the available fuel resources. Consider the following example: a man starts to run 5 km every day and soon discovers that he can complete the same distance within the same amount of time (*e.g.*, 0.5 h) but with a lower heart rate. His body has adapted to this cardiovascular stress physiologically, biochemically, and even anatomically in the long run, thus becoming a more efficient fuel utilizer; his body is able to achieve the same running average speed (5 km/0.5 h = 10 km/h), while utilizing less fuel. However, every time his body oxidizes 1 g of glucose while running, the heat released by his body continues to be ~4 kcals, which will not change as he ages or as a function of his genome, epigenome, or proteome.

22. The Coca-Cola Company and their insidious marketing arms

The Global Energy Balance Network (GEBN) was a US-based marketing arm of The Coca-Cola Company (hereinafter referred to as Coke), claiming to fund research on the causes of obesity[43]. GEBN's core message was that the primary cause of obesity is physical inactivity, not a poor diet[44-46]. In plain language, their message was that people can continue to enjoy high-carbohydrate junk food, including Coke's drinks, as long as they exercise enough to remain in "energy balance."

With around 1.4 billion inhabitants, China is the world's most populous country, so Coke has naturally taken interest in China's market. In Greenhalgh's article, she covered this topic[46], and her findings were as follows:

(i) Coke's main vehicle for influencing obesity science in China was the International Life Sciences Institute (ILSI), a Coke-sponsored marketing organization that masqueraded as a scientific organization and whose founding president Alex Malaspina was concurrently the vice president of Coke; a few years ago, the ILSI and Coke were practically synonymous;
(ii) ILSI's website emphatically spotlights their long commitment to scientific integrity, but as pointed by Greenhalgh, "[a] close examination of how the organization [ILSI] works in practice reveals a different picture"[46];
(iii) Coke, working through ILSI-Global and ILSI-China, succeeded in redirecting China's obesity science and policy to emphasize physical activity over dietary modifications.

In addition to GEBN and ILSI, Coke leveraged the authority of countless health organizations to spread this message. In Spain, for example, at least 74 health organizations were sponsored by Coke from 2010 to 2016, with a total investment above 6 million euros[47]. The main message was the same as with GEBN: "The most prevalent strategy was to focus on physical activity and sedentary behaviors as key obesogenic risk factors"[47]. Rey-López

et al. article[47] is an excellent discussion of Coke's main marketing strategies.

Coke has also utilized US-based governmental organizations in spreading its propaganda. For example, the Centers for Disease Control and Prevention (CDC) has had longstanding ties to Coke[46]. Barbara Bowman, the previous director of the CDC's Division for Heart Disease and Stroke Prevention, resigned after her emails with a former Coke executive were disclosed[48]. These emails proved that Bowman had advised the former Coke and industry association executive on how to influence the Director-General of the World Health Organization (WHO) to stop promoting taxes on sugar. Perhaps prompted by this incident, the CDC website currently states the following: "Frequently drinking sugar-sweetened beverages is associated with weight gain, obesity, type 2 diabetes, heart disease, kidney diseases, non-alcoholic liver disease, tooth decay and cavities, and gout, a type of arthritis. Limiting sugary drink intake can help individuals maintain a healthy weight and have healthy dietary patterns"[49]. However, with regard to individual cases, there is absolutely no reason to assume systematic abuses on the part of the CDC. In my opinion, the CDC website and other bulletins currently have reliable information on the subject.

Although not everyone would agree, the idea that some authoritative nutrition and obesity journals are mainly marketing channels for Coke and other companies that "live" on sugar may hold merit on the basis of the best available evidence collected in 2020, 2011, and 2022. However, this does not, in any way, mean that all the researchers who have had published in these journals are dishonest. Without truthful articles, these misguided journals would not be able to operate any longer. Nevertheless, there is sufficient evidence that these misguided journals have had a considerable detrimental effect on humanity, and thus require very careful legal scrutiny. When the lives and health of hundreds of millions of people are threatened with misinformation, it is a very serious crime. Since the subject, to some extent, falls outside the scope of this article, there is no need to discuss the matter further; however, more detailed information about the activities of these corrupt journals will be presented in the upcoming article.

That having been said, Noakes' recent work *Real Food on Trial: How the diet dictators tried to destroy a top scientist* is a recommended read[50]. This book presents the large-scale corruption in nutrition-related publications in an excellent way. In addition, Lustig's recent *work Metabolical: The Lure and the Lies of Processed Food, Nutrition, and Modern Medicine*[51] is also worth reading. The nutrition industry is clearly tainted from top to bottom. Many researchers are unaware that they are being misled by large corporations like Coke because of the clever marketing strategies they employ.

In essence, contrary to what sugar industry-sponsored "researchers" claim, "you cannot outrun a bad diet"[52].

23. Conclusion

In this paper, a new paradigm that paints a more accurate picture of the evolution of body weight is proposed: Chronic positive mass balance is the actual etiology of obesity, not positive energy balance. This opens up a completely new era in obesity research. By shifting to a mass balance paradigm of obesity, a deeper understanding of this disease may follow in the near future. The immediate result of such a shift is that feeding studies will be more accurate, as mass measurements do not suffer from various uncertainty factors, like energy measurements (*e.g*., DLW)[53].

The paradigm shift must begin. The importance of treating and preventing obesity must take precedence over the honor of researchers. At times, fundamental knowledge structures may turn out to be incorrect, and thus must be abandoned. "That is what fundamental novelties of fact and theory do. Produced inadvertently by a game played under one set of rules, their assimilation requires the elaboration of another set," as Kuhn stated in his classic work *The Structure of Scientific Revolutions*[54].

The rational mind's ability for biases, exaggeration, and cover up is the crux[55]. Rationality *per se* does not cause problems, but the rational mind is attracted to the greatest of sins, namely the tendency to think of the things one knows as absolute, "ultimate truths." Researchers celebrate their own theories, claiming that better ones, or ones outside of theirs, do not even have to exist. They begin from the basic assumption that all the most fundamental facts have already been proven beyond doubt, that is, nothing important has been left unexplored. This is sometimes the case, but from time to time, even "ultimate truths" change.

A paradigm shift is an intellectual revolution, accompanied by the chaos and fear inherent in revolution. Sacrifice is always required to correct a mistake, and if the mistake is significant, so must the sacrifice. When the new truth is denied over a long period of time, a significant amount of sacrificial debt may have already accrued. Some leading researchers in the field seem to have already accrued enough debt that they treat the mass balance approach like a plague. They mirror those "unfit to become devotees of knowledge" who refused to be any part of the "new truths" that contradict prevalent opinions, as portrayed in Nietzsche's statement in his classic work *The Gay Science*.

Nietzsche described above the phenomenon that later came to be called cognitive dissonance. The theory of cognitive dissonance proposes that people are averse to inconsistencies within their own minds[56]. More specifically, cognitive dissonance refers to the perception of contradictory information. If a person has been teaching things related to energy balance for decades, the magnitude of dissociation can be at a massive level. Despite this, it is worth considering the fact that if the etiology of obesity is misunderstood, it will have a detrimental effect on practically any type of obesity and weight management research.

Occam's razor (*novacula Occami*) also supports the mass balance approach. This principle states that entities should not be multiplied unnecessarily. By definition, all assumptions introduce possibilities for error. If an assumption does not improve the accuracy of a theory or model, its only effect is to increase the probability that the overall theory or model is wrong. What does a person measure when he/she stands on a bathroom scale? Is it his/her body mass or energy? It is obviously the amount of mass in his/her body. Why then do people continue to study body mass changes in the context of energy changes? Such a perspective only offers a rough second-hand estimate at best. The right starting point is to measure mass directly. As aforementioned, energy balance and mass balance are separate balances in the human body.

The key publications in the reference list and other references that can be found in them may be helpful for further information about the subject. A recent paper by Arencibia-Albite[1] is a recommended read, which should, at least in my humble opinion, provide new insights into this subject.

Acknowledgments

I would like to thank my family for their support and care as well as my colleagues for stimulating discussions.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The author declares no conflict of interest.

Author contributions

This is a single-authored paper.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

All data generated or analyzed during this study can be found in the sources cited in this article.

References

1. Arencibia-Albite F, 2022, The energy balance theory is an inconsistent paradigm. *J Theor Biol*, 550: 111240.

   https://doi.org/10.1016/j.jtbi.2022

2. Wikipedia. Living Review. Available from: https://en.wikipedia.org/wiki/Living-review [Last accessed on 2022 Aug 27].

3. Arencibia-Albite F, 2020, Serious analytical inconsistencies challenge the validity of the energy balance theory. *Heliyon*, 6: e04204.

   https://doi.org/10.1016/j.heliyon.2020.e04204

4. Sterner RW, Small GE, Hood JM, 2011, The conservation of mass. *Nat Educ Knowledge*, 3: 20.

5. Meerman R, Brown AJ, 2014, When somebody loses weight, where does the fat go? *BMJ*, 349: g7257.

   https://doi.org/10.1136/bmj.g7257

6. Kooijman SA, Kooi BW, Hallam TG, 1999, The application of mass and energy conservation laws in physiologically structured population models of heterotrophic organisms. *J Theor Biol*, 197: 371–392.

   https://doi.org/10.1006/jtbi.1998.0881

7. Arencibia-Albite F, Manninen AH, 2020, The energy balance theory: An unsatisfactory model of body composition fluctuations. *medRxiv*.

   https://doi.org/10.1101/2020.10.27.20220202

8. Arencibia-Albite F, Manninen AH, 2021, The mass balance model perfectly fits both Hall *et al*. Underfeeding data and Horton *et al*. Overfeeding data. *medRxiv*.

   https://doi.org/10.1101/2021.02.22.21252026

9. Hall KD, Sacks G, Chandramohan D, *et al*., 2011, Quantification of the effect of energy imbalance on bodyweight. *Lancet*, 378: 826–837.

   https://doi.org/10.1016/S0140-6736(11)60812-X

10. Kong Z, Sun S, Shi Q, *et al*., 2020, Short-term ketogenic diet improves abdominal obesity in overweight/obese chinese young females. *Front Physiol*, 11: 856.

    https://doi.org/10.3389/fphys.2020.00856

11. Hall KD, Bemis T, Brychta R, *et al*., 2015, Calorie for calorie, dietary fat restriction results in more body fat loss than carbohydrate restriction in people with obesity. *Cell Metab*,

22: 427–436.

https://doi.org/10.1016/j.cmet.2015.07.021

12. Manninen AH, 2022, A reanalysis of the highly important metabolic ward feeding data of Hall and colleagues: A brief report. *Authorea*.

https://doi.org/10.22541/au.166134987.70569518/v1

13. Diamond HA, 1990, Reasonable doubt: To define, or not to define. *Colum L Rev,* 90: 1716–1736.

https://doi.org/10.2307/1122751

14. Ludwig DS, Aronne LJ, Astrup A, *et al*., 2021, The carbohydrate-insulin model: A physiological perspective on the obesity pandemic. *Am J Clin Nutr*, 114: 1873–1885.

https://doi.org/10.1093/ajcn/nqab270

15. Watanabe M, Tozzi R, Risi R, *et al*., 2020, Beneficial effects of the ketogenic diet on nonalcoholic fatty liver disease: A comprehensive review of the literature. *Obes Rev,* 21: e13024.

https://doi.org/10.1111/obr.13024

16. Volek J, Sharman M, Gómez A, *et al*., 2004, Comparison of energy-restricted very low-carbohydrate and low-fat diets on weight loss and body composition in overweight men and women. *Nutr Metab (Lond)*, 1: 13.

https://doi.org/10.1186/1743-7075-1-13

17. Goss AM, Gower B, Soleymani T, *et al*., 2020, Effects of weight loss during a very low carbohydrate diet on specific adipose tissue depots and insulin sensitivity in older adults with obesity: A randomized clinical trial. *Nutr Metab (Lond),* 17: 64.

https://doi.org/10.1186/s12986-020-00481-9

18. Gepner Y, Shelef I, Schwarzfuchs D, *et al*., 2018, Effect of distinct lifestyle interventions on mobilization of fat storage pools: CENTRAL magnetic resonance imaging randomized controlled trial. *Circulation,* 137: 1143–1157.

https://doi.org/10.1161/CIRCULATIONAHA.117.030501

19. Hall KD, 2020, Challenges of human nutrition research. *Science*, 367: 1298–1300.

https://doi.org/10.1126/science.aba3807

20. Choi YJ, Jeon SM, Shin S, 2005, Impact of a ketogenic diet on metabolic parameters in patients with obesity or overweight and with or without Type 2 diabetes: A meta-analysis of randomized controlled trials. *Nutrients*, 12: 2005.

https://doi.org/10.3390/nu12072005

21. Zaki HA, Iftikhar H, Bashir K, *et al*., 2022, A comparative study evaluating the effectiveness between ketogenic and low-carbohydrate diets on glycemic and weight control in patients with Type 2 diabetes mellitus: A systematic review and meta-analysis. *Cureus*, 14: e25528.

https://doi.org/10.7759/cureus.25528

22. Young CM, Scanlan SS, Im HS, *et al*., 1971, Effect of body composition and other parameters in obese young men of carbohydrate level of reduction diet. *Am J Clin Nutr*, 24: 290–296.

https://doi.org/10.1093/ajcn/24.3.290

23. Mozaffarian D, 2022, Perspective: Obesity-an unexplained epidemic. *Am J Clin Nutr*, 115: 1445–1450.

https://doi.org/10.1093/ajcn/nqac075

24. Pontzer H, Raichlen DA, Wood BM, *et al*., 2012, Hunter-gatherer energetics and human obesity. *PLoS One*, 7: e40503.

https://doi.org/10.1371/journal.pone.0040503

25. Centers for Disease Control and Prevention (CDC), 2004, Trends in intake of energy and macronutrients--United States, 1971-2000. *MMWR Morb Mortal Wkly Rep*, 53: 80–82.

26. Ford C, Chang S, Vitolins MZ, *et al*., 2017, Evaluation of diet pattern and weight gain in postmenopausal women enrolled in the Women's Health Initiative Observational Study. *Br J Nutr*, 117: 1189–1197.

https://doi.org/10.1017/S0007114517000952

27. Ravussin E, Lillioja S, Knowler WC, *et al*., 1988, Reduced rate of energy expenditure as a risk factor for body-weight gain. *N Engl J Med*, 318: 467–472.

https://doi.org/10.1056/NEJM198802253180802

28. Das SK, Saltzman E, McCrory MA, *et al*., 2004, Energy expenditure is very high in extremely obese women. *J Nutr*, 134: 1412–1416.

https://doi.org/10.1093/jn/134.6.1412

29. Rimbach R, Yamada Y, Sagayama H, *et al*., 2022, Total energy expenditure is repeatable in adults but not associated with short-term changes in body composition. *Nat Commun*, 13: 99.

https://doi.org/10.1038/s41467-021-27246-z

30. Ruddick-Collins LC, Morgan PJ, Fyfe CL, *et al*., 2022, Timing of daily calorie loading affects appetite and hunger responses without changes in energy metabolism in healthy subjects with obesity. *Cell Metab*, 34: 1472–1485.e6.

https://doi.org/10.1016/j.cmet.2022.08.001

31. Westman EC, Yancy WS Jr., Humphreys M, 2006, Dietary treatment of diabetes mellitus in the pre-insulin era (1914-1922). *Perspect Biol Med*, 9: 77–83.

https://doi.org/10.1353/pbm.2006.0017

32. Hall KD, Farooqi IS, Friedman JM, *et al*., 2022, Reply to G Taubes, MI Friedman, and V Torres-Carot *et al*. *Am J Clin Nutr*, 116: 614–616.

https://doi.org/10.1093/ajcn/nqac163

33. Obradovic M, Sudar-Milovanovic E, Soskic S, *et al*., 2021, Leptin and obesity: Role and clinical implication. *Front Endocrinol (Lausanne)*, 12: 585887.

https://doi.org/10.3389/fendo.2021.585887

34. Ludwig DS, Dickinson SL, Henschel B, *et al*., 2021, Do lower-carbohydrate diets increase total energy expenditure? An updated and reanalyzed meta-analysis of 29 controlled-feeding studies. *J Nutr*, 151(3): 482–490.

https://doi.org/10.1093/jn/nxaa350

35. Guyenet SJ, Hall KD (2021) Overestimated impact of lower-carbohydrate diets on total energy expenditure. *J Nutr*, 151(8): 2496–2497.

https://doi.org/10.1093/jn/nxab213

36. Janssen JA, 2021, Hyperinsulinemia and its pivotal role in aging, obesity, Type 2 diabetes, cardiovascular disease and cancer. *Int J Mol Sci*, 22(15): 7797.

https://doi.org/10.3390/ijms22157797

37. Vidić V, Ilić V, Toskić L, *et al*., 2021, Effects of calorie restricted low carbohydrate high fat ketogenic vs. non-ketogenic diet on strength, body-composition, hormonal and lipid profile in trained middle-aged men. *Clin Nutr*, 40: 1495–1502.

https://doi.org/10.1016/j.clnu.2021.02.028

38. Roekenes J, Martins C, 2021, Ketogenic diets and appetite regulation. *Curr Opin Clin Nutr Metab Care*, 24: 359–363.

https://doi.org/10.1097/MCO.0000000000000760

39. Food and Drug Administration (FDA), 2022, Changes to the Nutrition Facts Label. Available from: https://www.fda.gov/food/food-labeling-nutrition/changes-nutrition-facts-label [Last accessed 2022 Aug 07].

40. Adult Obesity Prevalence Maps. Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion, Division of Nutrition, Physical Activity, and Obesity. Available from: https://www.cdc.gov/obesity/data/prevalence-maps.html [Last accessed 2022 Sep 27].

41. Feinman RD, Fine EJ, 2007, Nonequilibrium thermodynamics and energy efficiency in weight loss diets. *Theor Biol Med Model*, 4: 27.

https://doi.org/10.1186/1742-4682-4-27

42. Feinman RD, 2019, Beyond "a calorie is a calorie": An introduction to thermodynamics. In: Nutrition in Crisis: Flawed Studies, Misleading Advice, and the Real Science of Human Metabolism. United States: Chelsea Green Publishing.

43. Kmietowicz Z, 2015, Coca-Cola funded group set up to promote "energy balance" is disbanded. *BMJ*, 351: h6590.

https://doi.org/10.1136/bmj.h6590

44. Barlow P, Serôdio P, Ruskin G, *et al*., 2018, Science organizations and Coca-Cola's 'war' with the public health community: Insights from an internal industry document. *J Epidemiol Community Health*, 72: 761–763.

https://doi.org/10.1136/jech-2017-210375

45. Serodio P, Ruskin G, McKee M, *et al*., 2020, Evaluating Coca-Cola's attempts to influence public health 'in their own words': Analysis of Coca-Cola emails with public health academics leading the Global Energy Balance Network. *Public Health Nutr*, 23: 2647–2653.

https://doi.org/10.1017/S1368980020002098

46. Greenhalgh S, 2021, Inside ILSI: How Coca-Cola, working through its scientific nonprofit, created a global science of exercise for obesity and got it embedded in Chinese policy (1995-2015). *J Health Polit Policy Law*, 46: 235–276.

https://doi.org/10.1215/03616878-8802174

47. Rey-López JP, Gonzalez CA, 2019, Research partnerships between Coca-Cola and health organizations in Spain. *Eur J Public Health*, 29: 810–815.

https://doi.org/10.1093/eurpub/cky175

48. Hessari NM, Ruskin G, McKEE M, *et al*., 2019, Public meets private: Conversations between Coca-Cola and the CDC. *Milbank Q*, 97: 74–90.

https://doi.org/10.1111/1468-0009.12368

49. Centers for Disease Control and Prevention (CDC). Get the Facts: Sugar-Sweetened Beverages and Consumption. Available from: https://www.cdc.gov/nutrition/data-statistics/sugar-sweetened-beverages-intake.html [Last accessed on 2022 Sep 11].

50. Noakes T, Sboros M, 2019, Real Food On Trial: How the Diet Dictators Tried to Destroy a Top Scientist. United States: Columbus Publishing.

51. Lustig RH, 2021, Metabolical: The Lure and the Lies of Processed Food, Nutrition, and Modern Medicine. New York: Harper Wave.

52. Malhotra A, Noakes T, Phinney S, 2015, It is time to bust the myth of physical inactivity and obesity: You cannot outrun a bad diet. *Br J Sports Med*, 49: 967–968.

https://doi.org/10.1136/bjsports-2015-094911

53. Speakman JR, Yamada Y, Sagayama H, *et al*., 2021, A standard calculation methodology for human doubly labeled water studies. *Cell Rep Med*, 2: 100203.

https://doi.org/10.1016/j.xcrm.2021.100203

54. Kuhn TS, 1970, The Structure of Scientific Revolutions. 2nd ed. Chicago: The University of Chicago Press.

55. Peterson JB, 2018, 12 Rules for Life: An Antidote to Chaos. United States: Random House Canada.

56. Vaidis DC, Bran A, 2019, Respectable challenges to respectable theory: Cognitive dissonance theory requires conceptualization clarification and operational tools. *Front Psychol*, 10: 1189.

https://doi.org/10.3389/fpsyg.2019.01189