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The Wishnofsky Trap: How the Mass Balance Model Reveals Critical Blind Spots in Ultraprocessed Food Trials

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Abstract

A recent *Science* perspective by Magkos, Forde, and Robinson critically examined five randomized controlled trials on ultraprocessed foods (UPFs) and concluded that the evidence for a processing-specific effect on energy balance is weak. Their analysis exposed a deeper problem: the reliance on the Wishnofsky rule – a fixed tissue energy density of 7,700 kcal/kg – to translate weight change into energy imbalance. This rule, though widely used, is a statistical abstraction, not a physical constant. Here, I argue that the Wishnofsky rule constitutes a structural blind spot that prevents energy balance model (EBM)-based analyses from adequately accounting for water shifts, nitrogen balance, and the varying composition of tissue change. I apply the mass balance model (MBM) to reinterpret the five UPF trials and demonstrate that MBM – by tracking mass flows directly in grams and decomposing weight change into its true components (fat, lean mass, glycogen, water) – resolves the very ambiguities that the *Science* perspective identified. I conclude by outlining what an MBM-informed UPF trial should measure and argue that future feeding studies must move beyond the Wishnofsky rule to direct mass accounting to yield mechanistically interpretable results.

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1. Introduction: The Wishnofsky Rule as a Structural Blind Spot

A recent *Science* perspective by Magkos, Forde, and Robinson provided a sobering assessment of the evidence linking ultraprocessed foods (UPFs) to obesity [1]. By systematically examining five randomized controlled trials that compared UPF-rich diets with minimally processed diets [2–6], the authors concluded that "available randomized controlled trials provide weak support for an ultraprocessing-specific effect of UPFs on body weight regulation… that is independent of established nutritional determinants" [1].

Their analysis was rigorous and, in many respects, definitive. Yet, in the very act of critiquing the UPF evidence base, Magkos and colleagues inadvertently exposed a more fundamental problem – one that extends far beyond the UPF debate. That problem is the **Wishnofsky rule**.

First articulated in 1958 from a small number of short-term feeding studies, the rule posits that one pound of body weight gained or lost is equivalent to approximately 3,500 kcal (roughly 7,700 kcal per kilogram) [7]. *It has never been experimentally validated across the full range of dietary compositions, physical activity levels, and baseline body compositions to which it is routinely applied*. Despite its widespread use in dietary studies and clinical practice, it remains a statistical abstraction rather than a physical constant. The actual energy density of tissue change varies dramatically – from approximately 1,000–1,800 kcal/kg for lean tissue to approximately 9,400 kcal/kg for adipose tissue – depending on the relative proportions of fat, lean mass, glycogen, and water gained or lost [8].

When Magkos and colleagues applied the Wishnofsky rule to estimate that a UPF-rich diet would have needed to alter energy balance by approximately 500 kcal/day to produce the observed weight change – and then declared this magnitude "difficult to reconcile with known human

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physiology" – they were not rejecting the UPF hypothesis. *They were, in effect, rejecting the validity of the Wishnofsky rule itself.* The 500 kcal/day figure is an artifact of an assumed constant that does not hold in practice.

Here, I argue that the Wishnofsky rule is not merely an inconvenience but a structural blind spot. It prevents energy balance model (EBM)-based analyses from adequately accounting for water shifts, nitrogen balance, and the varying composition of tissue gained or lost. Applying the mass balance model (MBM), I reinterpret the five UPF trials and demonstrate how MBM resolves the very ambiguities identified in the *Science* perspective.

2. Three Blind Spots of Wishnofsky-Based Interpretation

2.1. Water Balance: When the Scale Lies

Several of the UPF trials differed markedly in sodium content between the diet arms. In Preston *et al*., for example, the UPF-rich diet contained approximately 150% more sodium than the non-UPF diet [4]. Sodium is a primary determinant of extracellular fluid volume, and even modest differences in intake can produce measurable shifts in total body water within days.

Under the Wishnofsky rule, all weight change is automatically attributed to alterations in stored energy. Thus, the 1.35 kg weight gain observed over three weeks in the Preston *et al*. trial is converted into a presumed energy surplus of ~10,400 kcal, or roughly 500 kcal/day. However, if even 500 g of that weight gain was sodium-driven water retention rather than tissue accretion, the true tissue gain would be only 850 g. This reduces the implied energy surplus from ~500 kcal/day to ~315 kcal/day – a 37% difference arising solely from partitioning water from tissue, without any change in the underlying energy intake or expenditure data.

EBM-based analyses have no built-in mechanism to separate water from tissue components and can only speculate about “fluid retention.” In contrast, MBM treats water balance as an independent, directly measurable mass stream.

2.2. The Wishnofsky Rule Itself: A Statistical Abstraction, Not a Constant

The Wishnofsky rule implicitly assumes that all short-term weight change is composed of adipose tissue with a fixed composition. This assumption is demonstrably false. The composition of weight change varies systematically with diet type, exercise mode, baseline body composition, and phase of the intervention. Early-phase weight loss on a low-carbohydrate diet, for example, is dominated by glycogen depletion and its associated water release (3–4 g water per gram of glycogen) [9], not by fat loss. Applying the Wishnofsky rule during this phase systematically overestimates the true energy deficit.

The Wishnofsky rule persists not because it is accurate, but because it is convenient. It allows investigators to bypass the laborious metabolic measurements – 24-hour urine collections, indirect calorimetry, precise food weighing – that would be required to determine the actual composition of weight change. It is the dietary equivalent of assuming every object falls at the same speed regardless of mass: a useful first approximation that becomes actively misleading when precision is required.

MBM eliminates the need for this shortcut by decomposing weight change into its components directly from measurable mass flows. Fat loss is determined from carbon balance (dietary carbon minus exhaled CO_2 and fecal carbon). Lean tissue loss is determined from nitrogen balance. Water balance is determined from fluid input–output measurements. Glycogen-associated water shifts are explicitly modeled. No Wishnofsky assumption is required.

2.3. The Protein Leverage Puzzle: Why Nitrogen Balance Matters

In all five UPF trials, absolute protein intake (g/day) remained nearly identical between diet arms, even when total energy intake differed by 500–800 kcal/day [1]. This pattern is consistent with

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the protein leverage hypothesis [10] and underscores a core MBM principle: the body appears to regulate the mass of protein ingested, not merely the energy it carries.

Yet without urinary nitrogen data, it is impossible to determine whether this identical protein intake was sufficient to maintain nitrogen balance. If participants in one arm were in negative nitrogen balance – catabolizing their own lean tissue to meet amino acid needs – this would produce effects invisible to the Wishnofsky rule. Lean tissue loss lowers the overall energy density of weight change (lean tissue is ~80% water and has far lower energy density than fat), and the excreted nitrogen represents a direct mass outflow that standard EBM approaches do not track.

3. What an MBM-Informed UPF Trial Would Measure

The five UPF trials reviewed by Magkos and colleagues were methodologically strong by conventional standards. From an MBM perspective, however, they left several critical variables unmeasured. An MBM-informed trial would incorporate the following key measurements in addition to standard protocols [11]:

1. Precise mass intake quantification – All foods and beverages weighed to ±0.1 g, with macronutrient composition verified by laboratory analysis rather than database estimates.

2. Respiratory gas exchange via indirect calorimetry to determine daily carbon outflow (VO_2 and VCO_2).

3. 24-hour urine collections with total nitrogen quantification to calculate daily nitrogen balance and net protein accretion/loss.

4. Complete fecal collections (or validated markers) for net absorbed macronutrient mass.

5. Comprehensive water balance – tracking all water inputs and outputs, including insensible losses.

I recognize that the measurements described above are more resource-intensive than standard trial protocols. However, the cost of ambiguity is arguably higher. The five UPF trials reviewed by Magkos *et al*. collectively enrolled nearly 140 participants and required years of investigator effort and millions of dollars in research funding [2–6]. Adding MBM-consistent measurements to even a subset of these trials would have yielded data capable of resolving the mechanistic questions that remain unanswered. The incremental cost of 24-hour urine collections and indirect calorimetry is modest relative to the total cost of large feeding trials, and the return on investment – in the form of interpretable, mechanistically transparent results – is substantial.

With these measurements, the interpretation of a UPF trial would shift from "the UPF diet caused a weight gain of 1.35 kg, implying a 500 kcal/day energy surplus" to "the UPF diet caused a net accumulation of X g fat, Y g lean tissue, and Z g water." The Wishnofsky rule would become unnecessary, and the mechanistic basis of the observed changes would be transparent.

4. Conclusions: Beyond the Wishnofsky Rule

Magkos, Forde, and Robinson provided a valuable service by exposing the interpretive fragility of the current UPF evidence base [1]. That fragility, however, is not unique to ultraprocessed foods. It is a direct consequence of continued reliance on the Wishnofsky rule – a convenient statistical approximation that has long been mistaken for a physical constant.

The mass balance model offers a clearer path forward. By replacing indirect, assumption-heavy energy accounting with direct mass flows, MBM eliminates the Wishnofsky rule entirely and reveals precisely what weight change is composed of: grams of fat, grams of lean tissue, and grams of water.

For the UPF field, the way forward is clear. Future trials should move beyond the Wishnofsky rule and adopt direct mass accounting. Only then will we be able to answer the question that Magkos and colleagues rightly posed – whether there is an effect of ultraprocessing on body weight regulation that is independent of established nutritional determinants – with the mechanistic precision the question deserves.

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The Wishnofsky rule has served as a useful shorthand for nearly seven decades. But convenience is not the same as correctness. The time has come to retire it and replace it with the direct mass accounting that the MBM provides.

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