# A reanalysis of the highly important metabolic ward feeding data of Hall and colleagues: a brief report

Anssi H Manninen[1]

[1]Affiliation not available

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Anssi H Manninen, Research & Development, Dominus Nutrition Oy, Raahe, Finland.

Corresponding author: Anssi H Manninen, Dominus Nutrition Oy, Ylipäätie 438, FIN-92220, Raahe, Finland. Email: anssi@dominusnutrition.fi

**Abstract**

**Background & Aims**

There is an ongoing debate about the role of macronutrient distribution in weight management.

The purpose of this brief report is to reanalyze the metabolic ward feeding data of Hall et al. (Cell Metab. 2015 Sep 1;22(3):427-36).

**Results**

I inevitably came to the conclusion that these diligent and well-meaning researchers were misinterpreting the research data. Their data actually demonstrate that a carbohydrate restricted diet show no risk of body fat accumulation.

**Conclusion**

The purpose is not to attack any group of researchers, but it is necessary to correct misinterpretations that are highly important for public health. The bottom line is that a carbohydrate restricted diet leads to greater body mass and fat mass loss than isocaloric fat restricted diet.

Keywords: macronutrients, body weight regulation, obesity, energy balance theory, mass balance model

**Introduction**

"A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it."

– Max Planck

In 2015, Kevin Hall and colleagues published a highly influential paper entitled "Calorie for Calorie, Dietary Fat Restriction Results in More Body Fat Loss than Carbohydrate Restriction in People with Obesity" in a highly respected journal *Cell Metabolism* [1]. The authors restricted dietary carbohydrates *vs* . dietary fat for 6 days following a 5 days baseline diet in 19 obese adults confined to a metabolic ward where they exercised daily. Subjects were given both isocaloric diets, the carbohydrate restricted diet (RC; i.e., a low-carbohydrate diet) or the fat restricted diet (RF; i.e., a high-carbohydrate diet), in random order during each of two stays in a ward. For macronutrient content of the baseline, RC and RF, see Table 2 in [1].

Data seems to suggest that that the RF resulted in a greater rate of body fat loss compared to isocaloric RC. As this paper has had very significant implications for global nutrition policy, I decided to take a closer look and reanalyze the Hall *et al* . data.

**Hall *et al.* data demonstrate that carbohydrate restricted diet (RC) shows no risk of body fat accumulation**

The widely accepted energy balance theory (EBT; "Calories In, Calories Out") postulates that body fat fluctuations are the consequence of the imbalance between dietary fat consumption and net fat oxidation. Accordingly, the RF is expected to result in a greater fat loss than an isocaloric RC, as fat intake is substantially lower. *It should be noted, however, that this is a reasonable hypothesis only if the net fat oxidation is independent of diet´s macronutrient distribution* . If the net fat oxidation increases as fat intake increases (and *vice versa* ), fat loss can be similar among isocaloric diets that vary greatly in dietary fat content. Hall *et al* .´s respiratory quotient (RQ) data demonstrate that this is indeed the case, as their Figure 2C indicate that fat oxidation increases in proportion to dietary fat intake. Consequently, *the characteristic high fat content of the RC elicits higher levels of fat oxidation, which counterbalances the high fat intake avoiding excessive body fat deposition* . This interpretation must be valid, as dual-energy X-ray absorptiometry (DXA) data presented in their Table 3 indicate that fat loss in the RC was similar to that of the RF even though the latter diet contained substantially less fat (fat intake: RC = 108g/day *vs* . RF = 17g/day; fat loss: RC = –0.529±0.13kg *vs* . RF = –0.588±0.14kg, p = 0.78). Therefore, it seems clear that alleged risk of body fat accumulation with RC diets is highly unlikely.

**The cumulative fat measurements reported are artificial quantities that do not reflect the *actual* level of body fat loss**

DXA measurements in Hall *et al* . study are the only *direct* measurement of fat loss. The presented cumulative fat loss illustrated in Table 3 (or in Figure 3D) is an undirect estimate of fat loss computed according to following equations (in grams):

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

where Daily Net Fat Oxidation is another estimate calculated by

(Daily Net Fat Oxidation) = $1.63VO_2 - 1.64VCO_2 - 1.84N$ (2)

where $VO_2$ and $VCO_2$ are the liters 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 which unavoidably increases the measurement inaccuracy* . Moreover, if an indirect measurement is indeed accurate, it should be very close to the most precise direct measurements available, such as dual-energy x-ray absorptiometry (DXA). Consequently, if cumulative fat loss calculations reported by Hall *et al* . are accurate, they should be nearly identical to values measured by DXA, which is clearly not the case. *The cumulative fat measurements illustrated in Table 3 (or Figure 3D) are thus artificial quantities that do not reflect the actual level of fat loss* .

As recently pointed by Arencibia-Albite, the EBT-based fat loss equation (1) ignores the fact that fat loss can also occur from the excretion of fatty acid derivatives [9]. However, there is no reason to dwell on the matter in this brief report, so I refer the reader to reference [9].

Nevertheless, Hall *et al* . try to convince readers that the direction of accuracy is other way around, i.e., cumulative fat calculations are more accurate than direct DXA fat mass measurements. In the justification of such a surprising proposal, they argue that DXA measurements may be prone to inaccuracies in settings of carbohydrate restriction as this may lead to greater water loss than fat restriction:

"But even high precision methods, such as DXA, may lack the sensitivity to detect small differences in body fat change… Indeed, retrospective analysis [what analysis?] of our data suggests that the minimal detectable difference between the diets for body fat mass using DXA was [?] 0.4 kg. Thus, we suspect that the DXA measurements of fat mass change in the present study were insufficiently sensitive to detect differences between the diets. Furthermore, DXA may provide inaccurate results in situations of dynamic weight change and shifting body fluids... This could be especially important with diets differing in their level of carbohydrate restriction since greater losses of body water are likely with lower levels of dietary carbohydrate." [1]

*It should be noted, however, that DXA fat mass measurements will be mainly unaffected since the amount of water present in the body fat compartment is very low* . Thus, if any inaccuracy is present, it would be substantially greater for lean mass measurements than for fat mass measurements as total body water is basically localized in the lean mass compartment. This fact alone refutes the abovementioned interpretation by Hall *et al* .

The sensitivity of the DXA instrument is hardly of practical importance in the treatment of obesity. Let's assume, as Hall *et al* . claim, that DXA sensitivity is 0.4 kg. This means that if DXA fat mass measurement before a dietary intervention is, let say 35 kg, and a particular underfeeding intervention decreases fat mass by exactly 200 g (0.2 kg) then DXA measurement will still read 35 kg, as the fat mass change is less than the sensitivity of the DXA instrument. Obviously, this is immaterial during typical underfeeding interventions, as in these situations the fat loss substantially exceeds the sensitivity of the DXA.

**Compared to the RF, the RC resulted in significantly greater body mass loss *both* experimentally and computationally**

Table 3 by Hall *et al* . shows that the RC resulted in substantially more body mass loss than isocaloric RF (RC:– 1.85 +- 0.15 kg *vs* . RF: –1.3 +- 0.16 kg, p = 0.022). For example, the simulation in their Figure 3H shows that, over a six months period, the RC leads to approximately 4 kg of extra body mass loss compared to the RF.

**The speculation about a greater loss of muscle mass in the RC is highly likely incorrect**

Hall *el al.* state: "Model simulations... implicated small persistent changes in protein balance resulting from the fact that dietary carbohydrates preserve nitrogen balance to a greater degree than fat" [1].

It should be noted, however, that a large body of evidence indicates that the RC is, if anything, *protective* against muscle protein catabolism, as already pointed out by this author in 2006 [7]. Simply put, ketone body metabolism by the brain displaces – at least partially – glucose utilization and thus spares muscle mass [7]. Furthermore, ketone bodies exert a restraining influence on muscle protein breakdown [7]. A recent review by Rondanelli *et al* . included 44 eligible studies and concluded that a very-low-carbohydrate diet preserves the fat-free mass during weight loss [8]. It is worth noting that bioelectrical impedance measurements may suggest a greater loss of lean body mass, but changes in total body fluid and electrolyte content, as a result of dietary ketosis, may complicate these measurements [7].

**Simulation according to the mass balance model (MBM)**

A growing body of evidence indicate that the widely accepted EBT ("Calories In, Calories Out) is a flawed paradigm. Instead, *it is becoming increasingly clear that body mass is regulated according to the "Mass In, Mass Out" principle* [2,3,4,5,6,9]. A very comprehensive and detailed review can be found in source [9], while a relatively easy-to-read and practical review can be found in [5]. Indeed, the results of this well-controlled feeding experiment by Hall *et al* . are also in full agreement with the mass balance model (MBM). In**Figure I** , I present a MBM simulation of Hall *et al.*data.

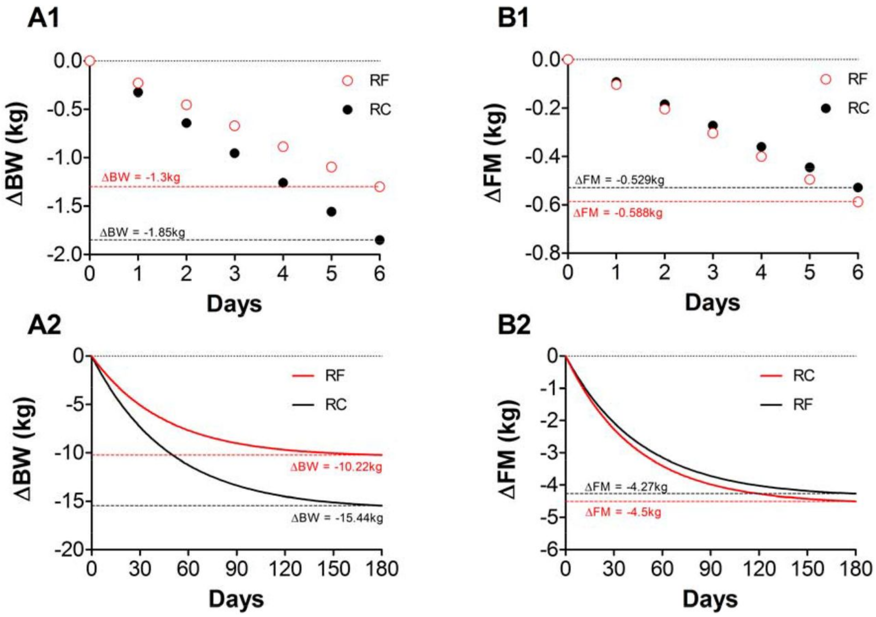


**Figure 1 . Mass balance model (MBM) simulation of Hall*et al.* data.** A1. MBM body weight (mass) trajectories perfectly match those reported by Hall *et al.* over the trial duration (6 days). A2. This graph shows the same body mass loss trajectories as in panel A1 but extended for 180 days. MBM predicts a greater body mass loss in the RC diet in contrast to the RF diet. B1. Fat loss trajectories that underlay weight loss in A1 perfectly match those reported by Hall et al. [3] over the trial duration (6 days). B2. This final graph shows the same fat loss trajectories as in panel B1 but extended for 180 days. For further details, please see [3]. BW = body weight (mass); FM = fat mass.

## Concluding remarks

The purpose of this reanalysis is not to attack any group of researchers, but experts and citizens should know that the results of this highly influential study have definitely been misinterpreted. And this has a very significant impact on public health. Their data actually demonstrate that the RC show no risk of body fat accumulation. *The important bottom line is that the RC leads to greater body mass and fat mass loss than isocaloric RF* . However, there is no reason to blame these well-meaning researchers of human error. Without their hard work this reanalysis would not have been possible.

## Conflict of interest

The author declared no conflict of interest.

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## Author contributions

The sole author was responsible for all aspects of this manuscript.

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## List of abbreviations

RC = carbohydrate restricted diet (i.e., a low-carbohydrate diet); RF = fat restricted diet (i.e., a high-carbohydrate diet); EBT = energy balance theory; MBM = mass balance model; RQ = respiratory quotient; DXA = dual-energy x-ray absorptiometry; BW = body weight; FM = fat mass.

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