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Energy Content of Weight Loss: Kinetic Features During Voluntary Caloric Restriction

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Abstract

Objective—The classic rule stating that restricting intake by 3500 kcal/wk will lead to a 1-lb/wk rate of weight loss has come under intense scrutiny. Generally not a component of most weight loss prediction models, the “early” rapid weight loss phase may represent a period during which the energy content of weight change (EC/W) is low and thus does not follow the classic “rule”. The current study tested this hypothesis.

Methods—Dynamic EC/W changes were examined in 23 CALERIE Study overweight men and women evaluated by dual-energy x-ray absorptiometry during weight loss at treatment weeks 4 to 24. Changes from baseline in body energy content were estimated from fat and fat-free mass. Repeated measures ANOVA was used to determine if EC/W changed significantly over time. The evaluation was expanded with addition of the Kiel 13-week weight loss study of 75 obese men and women to test with adequate power if there are sex differences in EC/W .

Results—The ANOVA CALERIE time effect was significant ($p < 0.001$) with post hoc tests indicating EC/W (kcal/kg) increased significantly from week 4 ($X \pm SEM$, 4, 858 ± 388) to 6 (6,

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DISCLOSURES

None of the investigators report conflicts of interest for this study.

AUTHOR CONTRIBUTIONS

Design SH, DT, CKM, LMR, ABW, MJM

Conduct SH, ABW, CKM, LMR, MJM

Data Collection SH, DT, CKM, LMR, BS, ABW, MJM, WS, AMN

Data Analysis SH, DT, CKM, LMR, BS, ABW, MJM, WS, AMN

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041±376, $p<0.01$) and changed insignificantly thereafter; EC/ W was significantly larger for Kiel women (6, 804±226) versus men (6, 119±240, $p<0.05$).

Conclusions—Sex-specific dynamic relative changes in body composition and related EC/ W occur with weight loss initiation that extend one-month or more. These observations provide new information for developing energy balance models and further define limitations of the 3500 kcal energy deficit 1 lb weight loss rule.

Keywords

Energy Balance; Body Composition; Weight Loss; Body Fat

INTRODUCTION

Wishnofsky's "rule", one pound of weight loss is equivalent to a deficit of 3500 kcal (i.e., 7700 kcal/kg) [1, 2], is one of the most pervasive in clinical nutrition and medicine. Widely cited in scientific reports, textbooks, and on credible websites [3, 4], this half-century old common wisdom states that the compliant subject will shed 1-lb/week or 52 pounds/year simply by reducing intake by about 500 kcal/d.

An appropriate main criticism of Wishnofsky's rule is that as subjects lose weight reductions in energy expenditure reduce the imposed energy deficit and slow the rate of weight loss [5–14]. Lowering intake by 500 kcal on diet day one closely approximates an energy deficit of -500 kcal, but the magnitude of this deficit and associated weight loss decrease markedly over time. Loss of energetically-active tissue [5], metabolic adaptations [11, 12, 15], and a reduced cost of weight-related energy expenditure [6, 13, 16] account for the self limiting nature of weight loss.

A second criticism of Wishnofsky's rule is that voluntary diet induced weight loss composition depends on the subject's initial body composition [8, 17, 18]. With negative energy balance, obese subjects lose mainly energy-dense fat while lean subjects lose relatively large amounts of low energy content fat-free mass (FFM) [8, 17, 18]. Although experiencing a "healthier" composition of weight loss, to lose one pound requires an obese subject to lower their energy intake more than that of a lean subject [8, 10].

Remarkably little recent collective information is available in this context on another widely recognized response to dieting: the relatively large early rapid weight loss accounted for by dynamic changes in glycogen, protein, and fluid balance [11, 19]. Often viewed as transient and inconsequential, this "early" weight loss effect would predictably reduce the energy content of weight loss far below that of Wishnofsky's rule. Dieting obese subjects reducing their intake 500 kcal/d would experience more rapid early weight loss than expected based on a 3500 kcal/lb energy content of weight change. Later marked slowing of weight loss, despite continued rigorous diet adherence, is one reason for subject disappointment, frustration, and ultimately relapse [20].

The present study extends the pioneering studies of Dole et al. [21], Grande [22], and Forbes [23] on the early period of voluntary weight loss. Dole et al. in 1955 [21] reported a low energy content of weight change (2500 kcal/kg) over 4 days in dieting obese women. Grande's 1959 review described a composite view of weight loss energy content over 24 weeks that included combined data from his own studies in normal weight men with those of other investigators [22]. As with Dole et al. [21], the energy content of early weight loss (i.e., first several weeks) appeared lower than that of later weight loss. Forbes' in 1970 [23] first articulated the mathematical concept of an early rapid weight loss phase followed by a slower longer period of weight loss. Forbes later showed that the composition of long term

weight loss differs between lean and obese women [17], thus leading to some uncertainty about the interpretation of Grande's observations in normal weight men [22]. Moreover, a large proportion of earlier weight loss studies were carried in obese women who may respond differently to interventions in men, a concept supported by the observation that men tend to lose more lean than women during periods of negative energy balance [24].

Herein, we report the first systematic study ranging from 4 to 24 weeks that specifically examines the energy content of early weight loss kinetics among subjects ranging from overweight to obese.

METHODS

Our aim in conducting this study was two-fold: to provide new clinically-relevant information on the early weight loss phase; and to fill an important information gap needed for developing human dynamic energy balance models. The energy content of weight loss observed during the early phase of dieting was examined in two data sets extending between 4 and 24 weeks of voluntary caloric restriction (CR).

The core analytical strategy was to evaluate the kinetics of body composition and thus energy content change in Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE) Study participants enrolled in the Phase I study at Pennington Biomedical Research Center. The CALERIE Study was approved by the Institutional Review Board and all subjects signed an informed consent prior to participation. The comprehensive CALERIE Study (25, 26) included healthy men and women prescribed low energy diets and who were then evaluated with dual-energy X-ray absorptiometry (DXA; QDR 4500A, Hologic, Bedford, MA) for changes in fat and fat-free mass (FFM) at treatment weeks 4, 6, 10, 12, 22, and 24. The observed changes in fat and FFM were used to estimate changes in total body energy content and the energy content of weight loss, calculated as total body energy content/ body weight at each respective time point.

Two CALERIE diet groups were pooled in these analyses, the first including subjects placed on CR (25% diet-imposed energy deficit) and the second on a very low calorie diet (VLCD, 890 kcal/d until 15% weight loss, then a weight maintenance diet). The CALERIE participants were ethnically-mixed men (age <50 yrs) and women (<45 yrs) who were randomly assigned to the weight loss groups.

The CALERIE data at weeks 4, 6, 10, 12, 22, and 24 were utilized in a repeated measures analysis of variance (ANOVA) to determine if the energy content of weight loss changed significantly over time. Data were derived from the two CALERIE treatment groups with treatment group included in the model. Post-hoc tests (repeated contrasts) were used to determine if the energy content of weight loss differed from time point to time point (e.g., from week 4 to 6, 6 to 10, etc.). This analysis had ample statistical power to determine if the energy content of weight loss differed over time (observed power > 0.99), though the analysis was not appropriately powered to detect a sex effect (observed power = 0.29) or a sex by time interaction (observed power = 0.17). Data were therefore examined in a secondary analysis from the larger available Kiel Study. The Kiel Study included obese men and women treated for ~13 weeks with a liquid VLCD (800–1000 kcal/d; BCM®-Diät, PreCon, Darmstadt, Germany)[19]. Body composition was evaluated before and following weight loss using a Hologic Discovery A (Hologic Corp., Bedford, MA) DXA system and whole-body-software version 12.6.1:3. A t-test was conducted to determine if the energy content of weight loss differed by sex. The t-test was adequately powered to detect a sex effect with an observed power >0.90.

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Statistical Methods

The energy content of weight loss was calculated from the losses of fat and FFM over the weight loss period assuming respective energy densities of 9.3 kcal/g and 1.1 kcal/g [15]. The energy density of FFM cited in the literature ranges from 1.1 kcal/g [16] to 1.8 kcal/g [10]. The computations arising from the various published FFM energy density parameters does not affect the major conclusions of the present study. With the exception of the t-test, all statistical analyses were conducted using SPSS, Version 18 (SPSS Inc., Chicago, Illinois). Alpha was adjusted to 0.01 to control for alpha inflation due to multiple testing. Results are expressed as $\bar{X} \pm \text{SD}$ in the tables and as $\bar{X} \pm \text{SEM}$ in the text and figures. Data presented in the figures were empirically fit with logarithmic functions that maximize line fit for visual presentation.

RESULTS

Subjects

The subject characteristics from the two studies are presented in Table 1. The CALERIE Study included 23 subjects, 10 men and 13 women. The men and women were similar in age and BMI, ~39 yrs (range 26–49 yrs) and ~28 (21–31) kg/m², respectively (both $p = \text{NS}$). Total weight loss over the 24 weeks was ~10 (3.6–15) kg (Table 2).

There were 75 total subjects in the Kiel Study, 15 men and 60 women. Men were older than the women (~38 [27–47] yrs vs. 34 [19–46] yrs, $p < 0.05$) and both groups had a similar BMI of ~35 (25–43) kg/m². Body weight decreased over the 13 weeks of study by ~13 (3.9–19.2) kg in men and ~8 (1.6–19.3) kg in women.

Compartmental Kinetics

The time main effect from the repeated measures ANOVA on the CALERIE Study was significant, $F(3.2, 66.8) = 17.00$, $p < 0.001$, indicating that the energy content of weight loss changed over time (Figure 1). The time by group interaction was non-significant, $F(3.2, 66.8) = 1.03$, $p = 0.39$. Post hoc tests indicated that the energy content of weight loss increased significantly from week 4 (4, 858±388 kcal/kg) to 6 (6, 041±376 kcal/kg), $F(1, 21) = 12.07$, $p < 0.01$, and did not change significantly thereafter (no other repeated contrasts were significant). The kinetic pattern in the energy content of weight change was the same in both CR and VLCD groups (Supplementary Figure S1).

The increasing energy content of weight loss observed over time implies temporal changes in the fractional contributions to weight (W) loss as fat and FFM. As shown in Figure 2, the fraction of weight loss as FFM fell steeply with time from 0.60±0.06 in men and 0.50±0.07 in women at Week 4 to values of FFM/ W of about 0.35±0.05 and 0.24±0.03 in men and women, respectively at Week 24. The corresponding values for fat/ W for men and women at Week 4 were 0.43±0.06 and 0.48±0.07 and at Week 24 were 0.66±0.05 and 0.75±0.03. Our observations, consistent across all weight loss groups, is that the energy content of weight loss is remarkably low during the early weight loss phase and moves towards the Wishnofsky's rule level after several weeks or even months of dieting.

The t-test conducted on the Kiel Study indicated the energy content of weight loss was significantly higher for women compared to men ($p < 0.05$) (Table 2). Women also had a

consistently higher energy content of weight change across the 24 weeks of CR and LCD protocols of CALERIE (Figure S1).

Forbes [17] and more recently Hall [8] reported an association between baseline fat mass and the proportion of weight loss as FFM. To explore this further, we conducted exploratory analyses by plotting the energy content of weight loss versus baseline fat mass in the CALERIE subjects. There was an association observed across the six available time points, although the correlation became statistically significant ($p < 0.01$) only at week 12. Subject sex did not enter the regression model for predicting the energy content of 12-week weight loss after controlling for baseline fat mass. The association between 13-week energy content of weight loss and baseline fat mass was non-significant in the Kiel Study data set.

DISCUSSION

Wishnofsky's rule, 3500 kcal energy deficit = 1 lb weight loss, is widely cited in texts and on the internet [3, 4], even though the author acknowledged the rule's limitations more than fifty years ago [1, 2]. With the recent advance of metabolism mathematical modeling concepts, Wishnofsky's rule has attracted careful analysis as a potential component of energy balance and weight loss prediction models [6–14, 16]. The present study confirms the hypothesis that the energy content of weight loss is not "constant" at 3500 kcal/lb during the course of intentional weight loss, but remains in a dynamic state of change for at least several weeks following induction of negative energy balance.

The value of 3500 kcal/lb (i.e., 7700 kcal/kg) is approached during the later phase of weight loss, with significantly higher levels in women than men. Recently developed dynamic weight loss models, however, reveal that the energy content of weight loss is not constant even within sex groups over the long term (13, 14). Simple dynamic model estimates were suggested by Hall et al. (i.e., a 10 kcal/d energy intake change will lead to ~ 1 lb of weight change when the body weight reaches a new steady state; 14) and full model predictions can be found on recently installed web sites (<http://bwsimulator.niddk.nih.gov>; <http://www.pbrc.edu/the-research/tools/weight-loss-predictor>).

While our study is the first to specifically examine this question in carefully evaluated overweight and obese cohorts, earlier studies explored related body composition concepts using well developed measurement methods. The most comprehensive of these was the 1959 review by Grande [22] in which the author pooled data from his own experimental studies of healthy normal weight male soldiers and the studies of other investigators to create a composite view of voluntary weight loss effects. Changes in body composition and energy content were computed from water (deuterium dilution space), protein (nitrogen), and fat (energy and weight) balances. We have reorganized Grande's data and plotted the mean results in Figures 3A (pooled studies) and 3B (Experiments 53 and 54 in normal weight men). The findings are remarkably concordant with CALERIE observations in overweight and obese men and women: a rapid increase in the energy content of weight loss is seen over 4–6 weeks, followed by slower positive increments over 24 weeks. The metabolic balance study of Dole et al. [21] examined the energy content of weight change over 4-day periods of weight gain and loss in obese women with an observed pooled mean of 2500 kcal/kg versus Wishnofsky's value of 7700 kcal/kg [1, 2]. Two additional short-term studies of our own are consistent with the findings of Grande [22] and Dole et al. [21]. de Jonge et al. [27] examined body composition changes by DXA in overweight men and women during a 3-week CR period. The observed energy content of weight loss was 3810 ± 858 and 5507 ± 1221 kcal/kg in men and women, respectively. Müller evaluated weight gain (overfeeding) and loss (CR) over 7 day intervals in the Kiel-II study in overweight men [28, 29] and observed a pooled energy content of weight change of 4720 kcal/kg (Figure 3B). Taken collectively,

these studies are fully consistent with our CALERIE results and indicate that the energy content of weight loss is not “fixed” at 3500 kcal/lb or 7700 kcal/kg as widely touted, but rather presents as a dynamic process with low values during the early period of CR that gradually increase and approach a plateau after several weeks or months.

By necessity, the energy content of weight loss must reflect corresponding relative changes in the rates of glycogen, protein, fat, and fluid loss. These compartments have differing half-lives and kinetic features during negative energy balance periods, although characterization in humans is limited as direct measurements are impractical over long time periods. The findings of the current six month study and that of our earlier comprehensive review [19] support at least what appears to be a two-phase weight loss model with an early period lasting several weeks and a later slower but longer second phase. The early weight loss phase is characterized by relatively large glycogen, protein, and fluid losses while the late weight loss phase typically has a high proportion of fat loss. Our observations on the energy content of weight loss are consistent with those of Forbes who first reported two phase mathematical models for nitrogen (i.e., protein) [30] and weight loss [23] during voluntary fasting or caloric restriction. Hall’s model includes a multi-scale equation describing changes in extra-cellular fluids [10]. Our findings indicate such a two-phase model is also appropriate for the energy content of weight change.

A second important observation of the current study is that the energy content of weight loss differed between men and women. This effect was evident in CALERIE and became statistically significant when observed in the larger Kiel Study. Men, by inference, therefore lose relatively more lean and less fat mass than women following CR. The current study findings strongly support our earlier observation in cross-sectional and longitudinal cohorts that the energy content of weight loss is larger in women than in men by about 20–25% [31]. This suggestion is also supported by the study of Chaston et al. [24] in which a systematic review found that for diet and behavioral weight loss interventions the fraction of weight loss as FFM tended to be larger in men ($X \pm SD$, $27 \pm 7\%$) than in women ($20 \pm 8\%$, $p=0.08$). Forbes applied available data in women to arrive at an empirical inverse association between baseline fat mass and the fraction of weight loss as FFM [17]. Hall substantiated Forbes’ empirical model supporting a curvilinear relation between baseline fat mass and the energy content of weight loss [8]. The Forbes-Hall approach suggests that men, with a relatively smaller baseline fat mass than women, will also have a smaller energy content of weight loss, a prediction borne out in the current study. We confirmed this prediction, but only at week 12 of the CALERIE study, with the observation that subject sex did not predict the energy content of weight loss after controlling for baseline fat mass. By contrast, the association between 13-week energy content of weight loss and baseline fat mass was non-significant in the Kiel Study. Our findings in CALERIE and Kiel studies highlight the likely multiple factors that determine the energy content of weight loss, including evaluation time point, the amount and range of baseline fat mass [4, 7], magnitude of caloric restriction [16], macronutrient intake, and level of physical activity [5, 12]. Controlling all or most of these variables while maintaining a high level of adherence is a challenge when conducting long term weight loss studies.

The current study results should be interpreted in the context of several limitations. First, we did not have very early weight loss data, notably in the first several days and weeks of the diet protocol. Generally, metabolic and energy balance methods [19, 21, 22] are optimally suited to capture very small early changes in body composition and are potentially more specific for evaluated compartments (e.g., protein) than are methods such as DXA, which was used in the current report [25–27]. Our results are fully complementary to those of Grande [22] and others [19, 21, 28] that were based largely on balance techniques. Second, we refrained in the current report from deriving specific kinetic parameters (e.g., half-life)

for the early composition of weight loss [19]. Parameters such as these have been derived for the rate of early protein (i.e., nitrogen) and weight loss by Forbes [23, 30], although in small subject samples. Also, it remains unclear which measurement approach is most appropriate and practical for estimating the energy content of weight loss during the early rapid weight loss period of CR [28]. Well designed studies using appropriate methodology and experimental protocols are needed to specifically examine this topic as a means of advancing the development of dynamic energy balance models.

The current report provides further evidence that with CR the energy content of weight change is not simply “3500 kcal/lb (i.e., 7700 kcal/kg)” and extends a growing literature on this topic [10, 12, 14, 16]. Specifically, we show that the energy content of weight loss observed in overweight and obese subjects begins low during the early period of CR and then gradually increases and approaches a plateau after several weeks or months. We also show that the energy content of weight loss differs significantly between men and women, at least in those with similar BMI. Our findings direct dynamic energy balance model development research by revealing the importance of the “early weight loss” period as defined by Forbes’ classic two-phase weight loss model (23). Patients should be advised of these effects so that they have realistic expectations related to their weight loss program.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

EC/ W	energy content of weight change
ANOVA	analysis of variance
CALERIE	comprehensive assessment of long-term effects of reducing intake of energy
CR	calorie restriction
DXA	dual-energy x-ray absorptiometry
NS	non-significant
SEM	standard error of the mean
VLCD	very-low calorie diet
W	weight

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Figure 1.

Energy content of weight change ($\Delta EC / \Delta W$, $X \pm SEM$) versus study week observed in CALERIE Study participants. The group mean values are fit with a logarithmic regression model (energy content of weight change (kcal/kg) = $1076 \times \ln(\text{time, weeks}) + 3767$; $R^2 = 0.88$, $p < 0.01$). The energy content of weight change increased significantly from week 4 to 6 ($p < 0.01$) and did not change thereafter.

Figure 2.

Fraction of weight loss as fat-free mass ($\Delta FFM / \Delta W$, $X \pm SEM$) versus study week observed in the CALERIE Study participants. The group mean values are fit with a logarithmic regression model in men (upper panel; energy content of weight change (kcal/kg) = $-0.13 \times \ln(\text{time, in weeks}) + 0.73$; $R^2=0.89$, $p<0.05$) and women (lower panel; energy content of weight change (kcal/kg) = $-0.14 \times \ln(\text{time, weeks}) + 0.63$; $R^2 = 0.84$, $p<0.05$).

Figure 3.

A. Energy content of weight change ($\Delta EC / \Delta W$) vs. study week plotted from the data compiled by Grande [22] across multiple studies. Data are mean study values. **B.** Energy content of weight change ($\Delta EC / \Delta W$) versus study day reported for Experiments 53 and 54 by Grande [22] and for the 7-day Kiel-II Study reported by Müller et al. [28, 29].

Table 1

Participant Group Characteristics.

Study (duration)	N	Age (yrs)	Weight (kg)	BMI (kg/m ²)	Fat (%)
CALERIE (24 wks)					
Men	10	38.0±7.3	88.3±9.1	28.2±1.4	24.3±4.0
Women	13	39.6±5.3	74.5±8.1 ^{††}	27.1±1.5	37.8±4.5 ^{††}
Kiel (13 wks)					
Men	15	37.8±5.9	112.7±12.7	34.4±3.7	27.8±4.1
Women	60	33.8±6.9 [†]	100.2±17.5 [†]	35.0±4.6	42.0±4.1 ^{††}

Results are mean±SD.

[†] p<0.05 and

^{††} p<0.001 for men vs. women. BMI, body mass index.

Table 2

Observed Changes in Weight and Body Composition.

Study (duration)	Weight (kg)	Fat (kg)	FFM (kg)	Energy (kcal)	E/ W (kcal/kg)
CALERIE (24 wks)					
Men	-9.7±3.6	-6.5±2.8	-3.1±1.6	-64, 249±26, 792	6, 500±1, 302
Women	-9.6±2.3	-7.1±1.8	-2.4±1.4	-69, 044±17, 051	7, 261±867 [†]
Kiel (13 wks)					
Men	-12.8±11.9	-7.6±2.7	-5.2±2.5	-76, 345±26, 047	6, 019±929
Women	-8.4±3.9 ^{†††}	-5.8±3.1 ^{††}	-2.5±1.9 ^{†††}	-57, 171±28, 804 ^{†††}	6, 804±1, 751 ^{†††}

Results are mean±SD.

[†] p=0.10,

^{††} p<0.05,

^{†††} p<0.001 for women vs. men. E, energy; FFM, fat-free mass; W, weight.