A computational model to determine energy intake during weight loss

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ABSTRACT
Background: Energy intake (EI) during weight loss is difficult and costly to measure accurately.
Objective: The objective was to develop and validate a computational energy balance differential equation model to determine individual EI during weight loss.
Design: An algorithm was developed to quantify EI during weight loss based on a validated one-dimensional model for weight change. By using data from a 24-wk calorie-restriction study, we tested the validity of the EI model against 2 criterion measures: 1) EI quantified through food provision from weeks 0–4 and 4–12 and 2) EI quantified through changes in body energy stores [measured with dual-energy X-ray absorptiometry (DXA)] and energy expenditure [measured with doubly labeled water (DLW)] from weeks 4–12 and 12–24.
Results: Compared with food provision, the mean (±SD) model errors were 41 ± 118 kcal/d and −22 ± 230 kcal/d from weeks 0–4 and 4–12, respectively. Compared with EI measured with DXA and DLW, the model errors were −71 ± 272 kcal/d and −48 ± 226 kcal/d from weeks 4–12 and 12–24, respectively. In every comparison, the mean error was never significantly different from zero (P values > 0.10). Furthermore, Bland and Altman analysis indicated that error variance did not differ significantly over amounts of EI (P values > 0.26). Almost all individual participants’ values were within CI limits.
Conclusion: The validity of the newly developed EI model was supported by experimental observations and can be used to determine an individual participant’s EI during weight loss. Am J Clin Nutr 2010;92:1326–31.

INTRODUCTION
The accepted reference for estimating habitual energy intake (EI) in free-living humans during energy balance is the doubly labeled water (DLW) method. DLW provides a measure of total daily energy expenditure (TDEE) with a CV of 5% (1), and, during a period of energy balance, TDEE is equal to EI. During periods of negative energy balance, however, DLW alone cannot estimate EI because TDEE is greater than EI. Thus, DLW must be combined with change in body energy stores to estimate EI.

EI that is assessed through summing changes in energy stores measured by dual-energy X-ray absorptiometry (DXA) and energy expenditure through DLW measurements provides the most valid estimate of EI during negative energy balance (2, 3). EI that is estimated through DXA/DLW measurements is more accurate than EI that is self-reported by the subject, which is typically grossly underestimated (4–6). Nonetheless, challenges of the DXA/DLW method lie in the limitation of DXA to measure small changes in body composition (4), cost, availability to researchers and clinicians, and participant burden.

We present a mathematical method for determining EI during weight loss based on a simple validated differential equation model for human weight change (7). The EI model requires input of baseline age, height, and sex and observed body weight at given intervals in time. The method builds on previous research (8) in which a 5-dimensional differential equation model was applied to estimate EI over intervals consisting of several months. Our current method builds on this approach by estimating sequential biweekly EIs, providing the first report of model assessed EI during weight loss for individual subjects, and supplying validation of the algorithm against food provision and EI quantified by the DXA/DLW method obtained from a recently conducted study of caloric restriction in overweight individuals (9). The developed model provides a new, practical, and low-cost opportunity to critically and noninvasively evaluate subject diet adherence and highlights important new areas for future research.

METHODS
Computational algorithm for EI
The foundation for the computational model for EI is a validated, one-dimensional, differential equation that predicts weight change as a result of both underfeeding and overfeeding (7). The dynamic equation (7) accounts for the changes in energy expenditure and the effect on energy stores on the basis of the current weight, height, sex, and age of the subject. The model is adjusted for the weight-related changes in resting metabolic rate and physical activity energy expenditure during negative and positive energy balance.

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The differential equation model is based on the human energy balance equation

\[ ES = EI - TDEE \]  

where \( ES \) represents the rate of energy stored or lost, \( EI \) represents the rate of EI, and \( TDEE \) represents the rate of total daily energy expenditure. Model terms were developed by using data and experimental conclusions from >10,000 subjects ranging in body mass indexes (BMIs; in kg/m\(^2\)) of 12 to 66. After input of an individual subject’s age, height, weight, sex, and target EI (kcal/d), the differential equation model predicted weight change with a mean error of 0.6 ± 2.2 kg at 6 mo. Therefore, knowledge of EI and TDEE yielded accurate information for the value ES. Our computational algorithm for EI applied the human energy balance equation to solve the inverse problem—namely, through knowledge of ES and TDEE we solved the value for EI.

The algorithm we developed considers biweekly weight during weight change as an imposed boundary value (constraining independent variable) with the trajectory (time course) determined by the differential equation. For each 2-wk interval, we start by entering the prescribed EI (kcal/d) and apply the established bisection shooting method for numerically solving a boundary value problem by repetitive iterations to hone the value of EI until it yields a predicted weight within a prescribed tolerance of the actual weight. This process is repeated to determine average EI over each 2-wk interval. The end result of the algorithm is a piecewise EI function defined over the course of the entire weight-change protocol. Specific details on model implementation appear in the supplementary materials under “Supplemental data” in the online issue.

The computational EI model was programmed by using Maple 12 computer algebra system software (2008; Maplesoft, Waterloo, Canada).

**Subjects**

The Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE) Study was approved by the Pennington Biomedical Research Center Institutional Review Boards (Baton Rouge, LA). All participants gave written informed consent before enrollment. The EI model’s validity was examined with data from phase I of the CALERIE trial, which tested the effects of calorie restriction on biomarkers of longevity. Data from subjects enrolled at the Pennington Biomedical Research Center were used. Twelve of the CALERIE phase I subjects were placed on a weight-maintenance diet, which began with a low-calorie diet (LCD) of 890 kcal/d, derived from liquid shakes, until 15% of baseline body weight was lost, followed by weight maintenance; 12 of the CALERIE phase I subjects were placed on a continuous 25% calorie-restricted (CR) diet, and 12 were prescribed a combination of continuous caloric restriction (12.5% calorie restriction) and exercise, which increased energy expenditure by 12.5%. The LCD participants achieved the 15% weight-loss goal and began the gradual reintroduction of solid food into the diet (refeeding) to maintain the 15% weight loss from weeks 5 to 12 of the study. The refeeding period lasted 2–5 wk. The body composition component of the differential equation model was constructed by using data that did not include exercise-induced changes to fat-free mass (FFM). Thus, the EI model’s validity was examined with data from participants who were reducing their weight solely through caloric restriction while maintaining their usual activity level: ie, the LCD and CR arms of the study (data for 23 subjects were included, because one LCD subject dropped out) (Table 1).

**EI criterion measures**

The validity of the EI model was tested against 2 criterion measures: 1) directly measured EI through food provided to participants by a metabolic kitchen and 2) EI measured with DXA and DLW.

**Criterion 1: food provision**

The first criterion measure consisted of EI measured through food provision and was separated into 2 periods: weeks 0–4 and weeks 4–12. CALERIE phase I subjects were provided with all of their food for these 12 wk of the study. During this period, participants ate 2 meals (breakfast and dinner) under supervision at the center each weekday, with lunch and snacks packaged for

### Table 1

Baseline cohort characteristics and experimental protocols

<table>
<thead>
<tr>
<th>Group</th>
<th>Duration (wk (n))</th>
<th>Baseline weight (Men (n = 10) Women (n = 13)) kg</th>
<th>Baseline BMI (Men (n = 10) Women (n = 13)) kg/m(^2)</th>
<th>Age (Men (n = 10) Women (n = 13)) y</th>
<th>Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-calorie diet</td>
<td>24 (11)</td>
<td>86.3 ± 7.7</td>
<td>28.5 ± 2.0</td>
<td>38.8 ± 10.3</td>
<td>Subjects provided with 890 kcal/d until 15% weight loss, then maintained weight maintenance.</td>
</tr>
<tr>
<td>Calorie restriction</td>
<td>24 (12)</td>
<td>90.1 ± 7.9</td>
<td>28.9 ± 1.0</td>
<td>37.5 ± 5.6</td>
<td>Subjects calorie restricted at 25% below baseline requirements.</td>
</tr>
<tr>
<td>Pooled cohort</td>
<td>24 (23)</td>
<td>88.6 ± 7.6</td>
<td>28.7 ± 1.4</td>
<td>38.0 ± 7.3</td>
<td>Weeks 0–4 and 4–12: EI from metabolic kitchen records; weeks 4–12 and 12–24: EI from DLW/DXA.</td>
</tr>
</tbody>
</table>

\(^{1}\) All aggregate values are presented as means ± SDs. EI, energy intake; DLW/DXA, dual-energy X-ray absorptiometry and doubly labeled water.
take-out. Weekend meals were also packed for take-out. Subjects were instructed to eat all food provided and not to consume any other foods or beverages. Participants were interviewed by trained registered dietitians each weekday to verify compliance with these instructions. The amounts of any provided foods that were not consumed, and foods (or calorie-containing beverages) consumed that were not provided, were carefully recorded to obtain an accurate estimate of actual EI. In addition, participants attended weekly group meetings led by a behavioral expert to foster adherence to the dietary regimen. During weeks 13 through 22, participants self-selected their diet on the basis of individual calorie targets.

Criterion 2: EI measured with DXA and DLW

The second criterion measure consisted of EI measured with DXA and DLW from weeks 4–12 and weeks 12–24. As part of the CALERIE phase I study, simultaneous DXA and DLW measurements were collected over a 2-wk interval at baseline and throughout weeks 4–5, 10–11, and 22–23 of the study. Subject EI was estimated from these measurements by approximating the value of ES through average changes in stored energy over time:

\[
\text{ES} \approx c_1 \left( \Delta FFM / \Delta t \right) + c_2 \left( \Delta F / \Delta t \right)
\]

where FFM represents kg of fat-free mass, \( F \) denotes kg of fat mass, and \( c_1 = 1100 \text{ kcal/kg} \) and \( c_2 = 9300 \text{ kcal/kg} \) are the energy densities of FFM and \( F \), respectively (10, 11). The value of TDEE was determined by using DLW measurements, and EI was estimated by summing the quantities for ES and TDEE.

Data analysis

The Bland-Altman approach (12) was used to compare the model estimates of EI against both criterion measures. Pearson’s correlation coefficients were calculated between model estimates and the criterion measures, followed by \( t \) tests to determine whether the model’s mean error differed from zero and regression analyses to determine whether error variance differed over levels of EI. All statistical analyses were performed with SPSS version 18 (SPSS Inc, Chicago, IL).

RESULTS

Model EI

The computational model was simulated by using baseline and biweekly weight measurements for each individual subject in the CALERIE phase I (9) study. Model simulations produced biweekly EI for each individual. Two example subjects are shown in Figure 1, one in the LCD group (Figure 1A) and the other in the CR group (Figure 1B). The subjects’ actual weight change at 2-wk intervals over the 24 study weeks is depicted by open circles. EI estimates, shown as solid squares, were derived by using the shooting method for solving a boundary value problem outlined in the supplementary materials under “Supplemental data” in the online issue. As expected, body weight increased only when EI exceeded the target energy requirements. Comparison of model estimates of EI to dual-energy X-ray absorptiometry and doubly labeled water estimates of EI during weeks 12–24 resulted in an absolute error <17 kcal/d for both subjects, which supports the finding that the subjects’ actual EI increased by amounts predicted by the model.

Criterion 1: food provision

EI estimated with the model correlated significantly with EI measured by food provision during weeks 0–4 (\( r = 0.99, P < \)
0.0001) and weeks 4–12 (r = 0.92, P < 0.0001; Figure 2, A and B). Compared with food provision, the model did not significantly over- or underestimate EI; the mean (±SD) errors were 41 ± 118 kcal/d [t(22) = 1.67, P = 0.11] and −22 ± 230 kcal/d [t(22) = −0.46, P = 0.65] from weeks 0–4 and 4–12, respectively (Figure 3). Importantly, nonsignificant regression slopes indicated that model error was consistent over amounts of EI from weeks 0–4 [R² = 0.000, F(1,21) = 0.009, P = 0.93] and weeks 4–12 [R² = 0.059, F(1,21) = 1.33, P = 0.26], with almost all subjects’ estimates falling within CI limits (Figure 3).

Criterion 2: EI measured with DXA and DLW

EI estimated with the model correlated significantly with EI measured by food provision during weeks 4–12 (r = 0.90, P < 0.0001) and weeks 12–24 (r = 0.90, P < 0.0001) (Figure 2, C and D). Compared with EI measured with DXA and DLW, the model did not significantly over- or underestimate EI; the model errors were −71 ± 272 kcal/d [t(22) = −1.24, P = 0.23] and −48 ± 226 kcal/d [t(22) = −1.01, P = 0.32] from weeks 4–12 and 12–24, respectively. Model error was consistent over levels of EI from weeks 4–12 [R² = 0.029, F(1,21) = 0.636, P = 0.43] and weeks 12–24 [R² = 0.017, F(1,21) = 0.354, P = 0.56], with all but one subject’s estimates falling within CI limits (Figure 3).

DISCUSSION

The computational model for EI was observed to produce valid estimates of EI when compared with EI measured with 2 criterion measures: food provision and DXA/DLW. As a result of this good agreement, use of the computation model appears to be a promising, inexpensive, and convenient method for estimating individual EI compliance during studies of negative energy balance. We note that because the forward model simulates weight change resulting from both underfeeding and overfeeding, the
The same approach can be applied to assess EI during overfeeding. The model estimated the EI actually provided to subjects during the first month of the study with a high level of accuracy and precision. Although DXA and DLW are the accepted standards for measurement of body composition and energy expenditures, they are not in perfect agreement with actual EI. We suggest that this is largely a reflection of the realities of measurement errors and individual biological variation. Thus, the analysis of agreement between the computational method and EI measured by DXA and DLW includes measurement error and biological variation for both measures. Moreover, the model was developed by using several regression formulas originating from DXA and DLW measurements; hence, the model estimates also contain similar variation in estimating EI.

The new EI model reveals weight-change effects, and its utility is clearly shown. First, the model shows that an increase in EI with noncompliance during the course of a weight-loss program does not necessarily result in weight gain unless a positive energy balance is achieved. For example, in Figure 1B, the subject’s EI increases from study weeks 14–20 by >1000 kcal/d. Nonetheless, the subject continued to lose weight, albeit at a slower rate, because EI did not exceed the kilocalorie target nor the energy requirement to maintain body weight at that point in the study. Conversely, body weight increased when the subject’s energy intake exceeds the kilocalorie target and energy requirements at week 18. Similar effects were observed as shown in Figure 1A: body weight increased only when the subject’s EI exceeded the kilocalorie target and the subject’s energy requirements that were dependent on body weight at that point in the diet. Interestingly, the model also suggests that a phenomenon generally observed in physics applies to body weight change. When body weight decreases rapidly (ie, at a high “velocity”), a large increase in EI is required to reverse the trajectory of body weight change (in this case, reverse weight loss and promote weight gain). This phenomenon appears to be detected by the model output (Figure 1A), although the model is also sensitive to much smaller perturbations in energy intake during periods of weight stability or relatively smaller changes in weight.

We validated the model’s capacity to accurately ascertain EI during negative energy balance through comparison to food provision and DXA/DLW data. A more rigorous validation of the model requires exact knowledge of EI during weight loss, which can only be determined if subjects are confined and their daily activity does not alter significantly from their free-living activity. We are not aware of any such studies, and given the expense, such a study is likely to be rare.

The challenge of lack of data on actual EI during negative energy balance can be overcome as more frequent DXA/DLW data are collected in ongoing and future weight-loss experiments. Our analysis using the CALERIE phase I study could then be...
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tested on data sets with a larger sample size that consist of a wider variance in BMI, age, height, and race. Further testing would indicate which population samples yield good model agreement with DXA/DLW estimates of EI and which population samples require model improvement.

A second limitation arises from measurement of EI at baseline and ES during weight change. As stated in the Introduction, during energy balance EI = TDEE. However, determining whether a subject is truly in energy balance requires simultaneous ES measurements to ensure that ES is equal to zero. In general, the 1- to 3-wk DLW observation interval to assess TDEE is too short to accurately measure ES using DXA. In fact, the most appropriate method for quantifying short-term body composition changes is the energy-metabolic balance method (13), which, to our knowledge, has yet to be applied in EI assessment. Although DXA measurements of ES are associated with modest measurement error, more precise measurements of ES for use in EI assessments present an important area for further study.

A final limitation of the current model is that it considers effects of changes in EI and not changes in physical activity beyond those expected from changed weight. Further developments to the model are required to incorporate the effects of exercise beyond that of usual activities. Vigorous training during periods of negative energy balance have important effects on the energy content of weight change (14, 15), which is a key model variable. Furthermore, adherence to 2 variables—exercise and EI—will need to be closely evaluated.

In conclusion, the study reported here describes the development and initial validation of a computational energy balance differential equation model to predict EI during negative energy balance. The dynamic model, based on thermodynamic principles, was shown to predict EI with a high level of accuracy and precision against EI measured from food provision and the combination of TDEE and changes in energy stores during a 24-wk study weight-loss intervention.

Due to an increasing prevalence of obesity, weight-loss interventions aimed at inducing negative energy balance are also on the rise. A major challenge treatment of obesity is to interpret the wide interindividual variability in body weight changes often reported in diet- and activity-induced weight-change experiments. A component of this variability is due to subject compliance levels to the specified intervention. As a result, investigators and clinicians need reliable methods to quantify subject adherence. The development and validation of computational models of body-weight and composition changes during intervention studies of weight loss provide a novel and practical tool for this application. Albeit still in the validation stage, the reported computational model has the potential for software- and web-based program development, providing ongoing EI data during weight loss to health care practitioners in real time. This application provides an important tool for monitoring adherence and implementing various strategies to foster successful weight loss.

The authors’ responsibilities were as follows—DMT, DAS, CKM, LMR, JAL, and SBH: designed the model validation; CKM and LMR: collected the data; DMT: developed the model; DAS, CKM, LMR, JAL, and SBH: contributed refinements to the model and estimated the parameters; DMT, DAS, CKM, LMR, JAL, and SBH: analyzed the data; DMT: prepared the first draft of the manuscript; and all authors: were responsible for revising the manuscript. None of the authors had a personal or financial conflict of interest.

REFERENCES