How large is the energy gap that accounts for the obesity epidemic?\textsuperscript{1,2}

Steven B Heymsfield

Humans are gaining excess weight, and alarmed scientists generally agree on the cause: positive energy balance beyond that needed to maintain a healthy weight. After all, body mass largely reflects a mix of water and energy-yielding organic chemicals, and when considered as a thermodynamic system, stores can only increase when substrate intake exceeds losses.

Agreement, however, stops beyond this simple conjecture, and a consensus is lacking on fundamental unanswered questions: What is the magnitude of “energy imbalance”? Can the energy imbalance be explained by excessive intake, reduced levels of physical activity, or a combination of both? Whereas these questions are debated among members of the academic community, their resolution has immense practical implications. By how much should people in developed nations reduce what they eat and increase the amount they exercise to “return” to weights before the “obesity epidemic” began? Public health efforts can be aimed at arresting or preventing weight gain by fostering actions aimed at achieving neutral energy balance and thus closing the “energy gap” (1).

Our questions could easily be answered if we had quantitative estimates of energy intake and expenditure, including that related to activity before the obesity epidemic and in the current population, particularly among those with excess adiposity. Food intake is highly variable from day to day, and available information on what people ate a half-century ago is based largely on inaccurate or biased self-report or food disappearance data (2). Activity estimates similarly are founded on self-report, observational studies, or indirect measures such as heart rate analyses, step counting, and fitness evaluations in selected populations. Because the energy imbalance causing the obesity epidemic is small for the population as a whole, in the range of several hundred calories per day, all agree that these approaches are far too imprecise to answer our questions with an acceptable level of accuracy.

Our ability to accurately quantify human energy intake and expenditure under nonlaboratory conditions only became available on a limited basis in the 1980s with the introduction of the doubly labeled water method (3). Subjects’ ingestion of 2 stable isotopes of water provided a means of quantifying total energy expended over a period of several weeks. When subjects are in near-energy equilibrium with stable weight over the study period, the measured expended energy is equivalent to ingested energy, and doubly labeled water evaluation provides an objective measure of calories ingested from food. The doubly labeled water method can be used to estimate energy expended in activity in which the investigator also measures subject resting metabolic rate (3). These types of objective data are lacking for populations before the obesity epidemic; in addition, doubly labeled water is costly and application so far includes only several thousand subjects participating in clinical trials in many laboratories throughout the world. New methods of quantifying energy balance components are now being introduced, but, at present, these important advances do not help us answer the energy imbalance questions.

The current controversy surrounds the definition of “energy gap” (1) and the means by which this energy imbalance is calculated. What happens to weight and energy expenditure if a person decides to increase his or her intake while maintaining a stable activity level? Positive energy balance and net protein and fat accretion with weight gain will follow. The creation of new molecules in addition to those created with daily turnover comes with a cost that is typically described as the “efficiency” of new substrate synthesis or tissue growth. The gain in weight and metabolically active cell mass will also impose an increase in the energy expended in activity and during rest. A new steady state weight will eventually be reached when all of these factors combine to achieve neutral energy balance.

What happens if this person reduces his or her activity level while maintaining a stable food intake? Positive energy balance with protein, fat, and weight gain will again follow. Food intake is “clamped” and will not change, although the subject will experience a weight-related increase in energy expended with activities and during rest. Weight gain will cease once the person reaches energy equilibrium.

We need to add yet another level of complexity when we consider children and adolescents. Variable levels of positive energy balance are present throughout the growth period, and normal growth must be accounted for when estimating the imbalance leading to overweight and obesity.

Subjects who gain excess weight are thus dynamically moving over time between various growth and nutritional “planes” with corresponding body composition and metabolic effects. These mass and functional changes can be exploited as energy imbalance biomarkers, and, through their measurement, investigators have used variable approaches in estimating the energy gap.

In 2003 Hill et al (1) were the first investigators to propose a definition of “energy gap” as the “required change in energy expenditure relative to energy intake necessary to restore energy

\textsuperscript{1} From Merck Research Laboratories, Rahway, NJ.
\textsuperscript{2} Address correspondence to SB Heymsfield, Center for Scientific Affairs, Merck Research Laboratories, PO Box 2000, RY34A-A238, Rahway, NJ 07065-0900. E-mail: steven_heymsfield@merck.com.

balance” (p. 585). By using back-of-the-envelope calculations, Hill et al estimated the rate of weight gain among adult CAR-DIA (Coronary Artery Risk Development in Young Adults) Study participants and then made 2 assumptions: an energy content of weight change of 3500 kcal/lb and a 50% efficiency of new substrate synthesis. Hill et al concluded that adult population weight gain could be eliminated by a combination of reducing intake and increasing energy expenditure by ≈100 kcal/d.

Applying a similar strategy, but in children and greatly refining Hill et al’s calculations, measurements, and evaluated samples to capture more of the relevant dynamic energy balance effects related to excess weight gain, Butte and Ellis (4), Wang et al (5), Butte et al (6), and Plachta-Danielzik et al (7) reported energy gaps that at the low end were similar to those reported by Hill et al (1) and at the high end several-fold larger. Comparing estimates is difficult, however, because the nature of evaluated subjects, measured variables, applied assumptions, and even the definition of energy gap varies across these studies.

Another approach to estimating the energy gap in children and adolescents was reported by Swinburn et al in 2006 (8), and their analysis strategy is extended to adults in their article in the current issue of the Journal (9). Assuming subjects are in energy equilibrium over several weeks, the authors estimated energy flux from doubly labeled water studies compiled by multiple research groups. When subjects are considered in balance, energy flux is equivalent to energy intake (I) and energy expenditure as measured by doubly labeled water. A weight (W) prediction formula was then derived by regression analysis that includes energy flux (ie, intake and expenditure), height, age, and sex as model covariates. Assuming height, age, and sex distribution are constant across subjects or populations, Swinburn et al’s “rule” states that W ∝ I 0.7 and (W2/W1) ∝ (I2/I1)0.7. If a subject instantaneously increases his or her energy intake by 5–6% (ie, the subject moves from I1 to I2), then his or her predicted weight increment will be ≈4%. Swinburn et al’s estimated energy gap that accounts for US population weight gain since the 1970s is several-fold higher (≈400 kcal/d) than that originally proposed by Hill et al (≈100 kcal/d; 1). This energy gap difference is not small, and recommendations on how to achieve a healthy population weight will strongly depend on which model, or for that matter which of any of the models now published we accept as the most valid.

A limitation of the approach of Swinburn et al (9) is the presentation of a statistical model that is population specific. For example, the US and Mexican Pima evaluated by Esparza et al (10) have roughly the same energy flux and should thus have the same weights, although the US Pima weigh 40% more than their Mexican counterparts. The discrepancy arises because the Mexican Pima are more active than the US Pima, and the 2 groups thus have different weight-energy flux functions. How weight and energy flux related to each other before the obesity epidemic is largely unknown because high-quality comparable data are lacking. There is substantial risk of error when applying the equations generated by Swinburn et al (9) outside of populations differing from that presented in the current study.

The report by Swinburn et al (9) and those of others attempting to define the energy gap magnitude provide us with a rich critical mass of information on which to build newer, more refined, and potentially more flexible models. The process of model building has yet another key beneficial effect for the field: it focuses us on the need for innovative measurement methods that can be widely applied in large long-term population studies.

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REFERENCES
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