Adjusting for energy intake—what measure to use in nutritional epidemiological studies?

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Background The measurement of energy intake in epidemiological studies is difficult. However, it is important that energy intake is assessed if epidemiological analyses are to correspond to isocaloric experiments. The aim of this study was to compare self-reported energy intake, physical activity, and body weight with energy expenditure measured by 4 days of heart rate monitoring with individual calibration of the relationship between heart rate and oxygen consumption.

Methods Volunteer sub-study of 97 men and women (mean ages 54 and 51 years respectively) within the European Investigation into Cancer (EPIC) study in Norfolk (UK). Dietary assessment of energy intake and physical activity was by self-report and weight was measured using standard techniques. Energy expenditure was assessed objectively by recording heart rate for 4 days following a calibration of the relationship between heart rate and oxygen consumption.

Results Self-reported energy intake by 7-day diary (mean 8.5 MJ/day) and food frequency questionnaire (FFQ) (mean 8.8 MJ/day) were significantly lower than objectively measured total energy expenditure (mean 11.2 MJ/day). The deattenuated partial correlations between total energy expenditure were 0.33 (7-day diary), 0.34 (FFQ), 0.50 (physical activity), and 0.56 (weight). Weight accounted for 31% (deattenuated) of the sum of squares about the mean of true energy intake after adjusting for age and sex. With the addition of self-reported physical activity, the model was significantly improved ($R^2 = 0.57$). Adding energy either assessed by the diary or FFQ did not improve the model.

Conclusions The results presented here indicate that to adjust for energy intake, for the purpose of replicating an isocaloric experiment in an observational epidemiological study, one would do considerably better adjusting for weight and physical activity, than adjusting for energy intake estimated from an FFQ.

Keywords Energy, physical activity, food diary, food frequency questionnaire, weight, validation, heart-rate monitoring

There is continuing high interest in epidemiology in identifying specific components of diet which may be related to specific health endpoints. The diet–disease relationships may be with the level of consumption of specific micronutrients, macronutrients, food groups, or particular foods. In each case, it will be important to demonstrate that the relationship is specific, and not a reflection of a more general association with total quantity of food consumed. It is generally accepted that associations between nutrients and disease should only be considered primary if the effects are independent of energy intake resulting from differences in body size, physical activity, and metabolic efficiency.1 That is, epidemiology should attempt to mimic the isocaloric requirement of experimental or metabolic studies. This has led to the practice of adjusting for total energy intake, as assessed by the dietary instrument used to generate the epidemiological data. The problem, however, is

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that the dietary instruments used in large-scale epidemiological studies may estimate energy intake rather badly. The most commonly used instrument in cohort studies of diet has been the food frequency questionnaire (FFQ) of Willett or adaptations of it, although diet record or diet diary methods are now being introduced. A recent large study compared energy intake assessed by the FFQ with energy expenditure measured by the doubly labelled water technique. The correlation between the FFQ estimate of energy intake and the ‘gold standard’ estimate of energy expenditure was 0.1 in women and 0.2 in men. Thus as a method of adjusting for true energy intake, adjusting for the FFQ estimate of energy intake is clearly inadequate. Energy intake has not been adjusted for to any appreciable extent. The results of an analysis adjusting for the FFQ estimate of energy intake cannot be considered as replicating an isocaloric experiment.

The main thrust of this paper is to examine whether there are better measures of energy intake that could be used. The paper reports a study nested within the European Investigation into Cancer (EPIC) study in Norfolk (UK) cohort in which heart rate monitoring was used as an objective method of estimating energy expenditure. The use of heart rate monitoring (HRM), with individual calibration of the relationship between oxygen consumption and heart rate, to estimate energy expenditure has been demonstrated to have good correlation (0.93) with the gold standard methods of doubly labelled water and whole body calorimetry. The technique was used in this study in order to compare self-reported energy intake by 7-day diary and FFQ, self-reported physical activity and weight. It is assumed that the errors in measurement and body weight are represented by partial correlation coefficients between various measures of energy intake and true energy expenditure obtained during the time the heart rate monitor was worn and the results remained substantially unchanged. Analyses were repeated using the minute-by-minute energy expenditure for each participant. Sleeping energy expenditure was calculated as 95% of basal metabolic rate (BMR) where this was derived from published prediction equations. Physical activity level (PAL) was computed for the 4 days as the ratio of total energy expenditure (TEE) to BMR.

Assessment of energy expenditure

Participants visited the clinic in order to undergo a standard protocol for individually calibrating heart rate against energy expenditure by indirect calorimetry. Following the individual calibration, volunteers wore the Polar heart rate monitor (Polar Electro, Finland) continuously during the waking hours for a period of 4 days. Heart rate readings were downloaded onto a database via a serial interface and the individual calibration data were used to predict minute-by-minute energy expenditure for each participant. Comparisons between TEE and PAL with self-report measures and body weight are represented by partial correlation coefficients (adjusted for age and sex) and deattenuated using reliability coefficients. We focused attention on correlation coefficients between various measures of energy intake and true energy intake, the reason being that this correlation reflects the extent to which confounding by true energy is accounted for by the measured variable in a linear regression. The relative contributions of the self-reported measures and body weight in explaining TEE are illustrated by the effect on $R^2$ in regression models, again deattenuated using reliability coefficients. All statistical computations were undertaken using Stata. Analyses were repeated using the minute-by-minute energy expenditure obtained during the time the heart rate monitor was worn and the results remained substantially unchanged.

Statistical methods

The reliability coefficients for PAL and TEE, using the HRM method, were 0.5 and 0.74 respectively as calculated from a previous study in which individually calibrated HRM was employed on four separate occasions over a 12-month period in a group with similar age, sex, and geographical structure.

Comparisons between TEE and PAL with self-report measures and body weight were represented by partial correlation coefficients (adjusted for age and sex) and deattenuated using reliability coefficients. We focused attention on correlation coefficients between various measures of energy intake and true energy intake, the reason being that this correlation reflects the extent to which confounding by true energy is accounted for by the measured variable in a linear regression. The relative contributions of the self-reported measures and body weight in explaining TEE are illustrated by the effect on $R^2$ in regression models, again deattenuated using reliability coefficients. All statistical computations were undertaken using Stata. Analyses were repeated using the minute-by-minute energy expenditure obtained during the time the heart rate monitor was worn and the results remained substantially unchanged. Similarly, analyses were performed with and without transformation of energy expenditure, weight, and energy

Methods

Setting and study participants

The EPIC study is based on a cohort of 500 000 volunteers from nine European countries with the aim of relating biomarkers and lifestyle to cancer and other chronic disease endpoints. The study reported here is a calibration sub-study embedded in the EPIC-Norfolk cohort and details of recruitment and measurement protocol have been previously reported. Dietary assessment of energy intake by the 7-day food diary (diary) and the semi-quantitative FFQ in the Norfolk study has been described in detail previously. Self-reported physical activity has been assessed throughout the EPIC study by the short EPIC physical activity questionnaire and individuals are classified according to a four-point physical activity index; inactive, moderately inactive, moderately active, and active. Over a period of 18 months 179 members of the Norfolk cohort took part in a validation study of dietary assessment by the FFQ and diary compared with urinary markers of nitrogen, potassium, and sodium. In addition to the collection of urine and the completion of questionnaires, energy expenditure was estimated by 4 days of heart rate monitoring (HRM) with individual calibration in 97 of the 179 participants. The diary, FFQ, and self-reported physical activity were completed, on average, 1.8 (SD 1.3) years before the objective assessment of energy expenditure.
intake from both the FFQ and diary; there was no marked difference between the results. Results reported are those for the untransformed variables.

Results

The characteristics of the volunteers in this study are described in Table 1, stratified by sex. Self-reported energy intake was significantly lower for both diary and FFQ when compared with TEE. For men, estimates of energy intake from the FFQ were lower than for the diary but for women energy intake was higher from the FFQ when compared with the diary. The ratio of energy expenditure in men to the energy expenditure in women was 1.28; the ratios of energy intakes in men to intakes in women were 1.25 for the diary estimates and 1.04 for the FFQ estimates. PAL was 1.72 (0.3) for both men and women.

Deattenuated partial correlation coefficients, adjusted for age and sex, between TEE and energy intake were 0.33 (P < 0.01) and 0.34 (P < 0.01) for diary and FFQ respectively (Table 2). The equivalent correlations between TEE and self-reported activity and body weight were stronger than for the dietary markers; 0.50 (P < 0.001) and 0.56 (P < 0.01) respectively. Partial correlations between PAL and self-reported behaviours were similar to those for TEE. However, PAL and weight were weakly correlated.

The partial R² for TEE with weight, physical activity, diary, and FFQ are reported in Table 3. This shows that weight accounts for 31% (deattenuated) of the sum of squares about the mean of true energy intake after adjusting for age and sex. Adding physical activity to the model improved the model significantly, producing an R² of 0.57. However, adding either the FFQ or the diary to the model including weight alone did not substantially improve the R² (0.38 and 0.39 respectively) or when either was added to the model including weight and physical activity (0.64 for both diary and FFQ).

Figure 1 illustrates mean values of TEE from heart rate by quintile of body weight, energy intake from FFQ and diary. The FFQ estimate of energy intake is almost independent of TEE, however, the diary does better, and weight is the most strongly associated with energy expenditure.

Figure 2 illustrates the positive association, adjusted for age and sex, between the self-reported physical activity index and PAL (test for monotonic trend, P < 0.001). The adjusted mean PAL in the inactive group is 1.58 (95% CI: 1.43, 1.73) and in the active group 1.94 (95% CI: 1.81, 2.07). The relationship between TEE and the physical activity index was also strong (monotonic trend P < 0.001) across the four categories (inactive group 9.93 MJ/day [95% CI: 8.8, 11.1], active group 12.8 MJ/day [95% CI: 11.9, 13.8]), adjusted for age and sex.

Table 2 Partial correlation coefficients (95% CI) between energy expenditure from heart rate monitoring (total energy expenditure [TEE] and physical activity level [PAL]) and self-reported energy intakes from dietary instruments, physical activity, and weight

<table>
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<tr>
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<th>TEE</th>
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<tr>
<td>Energy from diary (n = 97)</td>
<td>0.28** (0.09, 0.45)</td>
<td>0.33** (0.10, 0.52)</td>
<td>0.24* (0.04, 0.42)</td>
<td>0.34* (0.06, 0.59)</td>
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<td>Energy from FFQb (n = 94)</td>
<td>0.29** (0.09, 0.47)</td>
<td>0.34** (0.10, 0.55)</td>
<td>0.21* (0.01, 0.40)</td>
<td>0.30* (0.01, 0.57)</td>
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<td>Physical activity index (n = 78)</td>
<td>0.43*** (0.23, 0.60)</td>
<td>0.50*** (0.27, 0.70)</td>
<td>0.44*** (0.24, 0.60)</td>
<td>0.62*** (0.34, 0.85)</td>
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<tr>
<td>Weight (n = 97)</td>
<td>0.48*** (0.31, 0.62)</td>
<td>0.56** (0.36, 0.72)</td>
<td>0.11 (~0.09, 0.30)</td>
<td>0.16 (~0.13, 0.42)</td>
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a Deattenuated with reliability coefficient for total energy expenditure: 0.74.

Table 3 Partial R² (95% CI) with total daily energy expenditure from 4 days of heart rate monitoring, adjusted for age and sex

<table>
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<tr>
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<th>R² (95% CI)</th>
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<tr>
<td>Weight</td>
<td>0.23 (0.09, 0.37)</td>
<td>0.31 (0.12, 0.50)</td>
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<tr>
<td>Weight + physical activity</td>
<td>0.42 (0.21, 0.55)</td>
<td>0.57 (0.28, 0.74)</td>
</tr>
<tr>
<td>Weight + diary energy</td>
<td>0.29 (0.13, 0.43)</td>
<td>0.39 (0.18, 0.58)</td>
</tr>
<tr>
<td>Weight + FFQb energy</td>
<td>0.28 (0.12, 0.42)</td>
<td>0.38 (0.16, 0.57)</td>
</tr>
<tr>
<td>Weight + physical activity + diary energy</td>
<td>0.47 (0.26, 0.59)</td>
<td>0.64 (0.35, 0.80)</td>
</tr>
<tr>
<td>Weight + physical activity + FFQ energy</td>
<td>0.47 (0.25, 0.58)</td>
<td>0.64 (0.34, 0.78)</td>
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</table>

a Deattenuated with reliability coefficient for total energy expenditure: 0.74.

b Food frequency questionnaire.

* P < 0.05. ** P < 0.01. *** P < 0.001.
In conclusion, adjusting for energy intake is important in nutritional epidemiology. The precision and accuracy of the measurement of energy intake in nutritional epidemiology is critical to studying the role of energy as an exposure for disease risk and also for adjusting for its role as a confounding factor. In adjusting for energy intake in cohort studies, we are attempting to mimic an isocaloric experiment. However, dietary assessment of energy is not only difficult but the effects of measurement error in its assessment can have a significant impact on the results of a study. A poor estimate of energy intake will lead to distorted estimates of associations of other nutritional factors with health endpoints when adjusting for energy. Adjusting for strong confounding with a poorly measured confounding factor can be worse than not adjusting at all. With the relatively recent increase in media coverage and interest in the role that physical activity and inactivity may have with regard to the rising prevalence of overweight and obesity one should be cautious that differential reporting, which has plagued dietary assessment, might become evident in self-reported level of physical activity. The use of an objective method for estimating energy expenditure, which is less likely to be susceptible to the same differential reporting biases as dietary assessment, could prove to be a useful alternative for energy adjustment in nutritional epidemiology. The further development of the heart rate technique, to allow for less-intensive individual calibration, might make this method a viable option in an epidemiological setting.

This study suggests that both FFQ and diary are poor in predicting energy. However, body weight and a simple index of physical activity appear to correlate much better with energy. The results presented here indicate that to adjust for energy for the purpose of replicating an isocaloric experiment, one would do considerably better adjusting for weight, and perhaps additionally a physical activity index, than adjusting for an FFQ estimate of energy intake. The argument in favour of energy adjustment is that it may achieve a number of aims simultaneously, one of which is the partial control of measurement error. The inclusion in a diet–disease regression of two or more dietary factors, the errors in the estimated intakes of which are highly correlated, may substantially reduce the effect of measurement error on the regression coefficients. However, as shown in the companion paper, the effect on the regression coefficients may be highly unpredictable. There would not appear to be a single approach which most effectively exploits the multivariate error structure to reduce the impact of measurement error. Adjusting for an estimate of total energy intake may on occasion be ineffective.

In conclusion, adjusting for energy intake is important in analyses of nutritional epidemiological data to control the
confounding effects of energy intake and of body size. However, such adjustment may be better achieved by using weight, together with an index of physical activity if available, than by using an FFQ-derived estimate of energy intake. Adjusting for energy to correct partially for measurement error may often not be optimum, or even effective.

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References