Total daily energy expenditure among middle-aged men and women: the OPEN Study[1–3]

Janet A Tooze, Dale A Schoeller, Amy F Subar, Victor Kipnis, Arthur Schatzkin, and Richard P Troiano

ABSTRACT

Background: Few large doubly labeled water (DLW) studies have provided an objective measure of total energy expenditure (TEE) in free-living men and women. The committee that developed the 2002 Dietary Reference Intake (DRI) estimated energy requirements (EER) noted that DLW studies in adults aged 40 to 60 y were limited.
Objective: We aimed to describe TEE and physical activity energy expenditure in middle-aged men and women by sex, age, menopausal status, and level of obesity, and to compare TEE to the DRI EER.
Design: TEE was measured by the DLW method in 450 men and women aged 40–69 y from the Observing Protein and Energy Nutrition Study. Resting metabolic rate was estimated by use of the Mifflin equation.
Results: Unadjusted TEE was lower in women than in men (591 kcal/d); however, when the analysis was adjusted for fat-free mass, women had significantly higher TEE than did men (182 kcal/d). This difference appeared to be due to higher physical activity levels in women (physical activity energy expenditure adjusted for FFM was 188 kcal/d greater in women than in men). Mean TEE was lowest in the seventh decade. TEE from DLW was highly correlated ($r = 0.93$) with EER from the DRI equations.
Conclusion: In this population, TEE was higher in women than in men when adjusted for FFM, apparently because of higher physical activity levels in women. There were no significant differences in TEE, FFM, or physical activity levels in women by menopausal status. TEE was inversely associated with age and increased linearly with body mass index. This study corroborates the use of the DRI equations for EER. *Am J Clin Nutr* 2007;86:382–7.

KEY WORDS Total energy expenditure, doubly labeled water, dietary reference intake, estimated energy requirement

INTRODUCTION

Energy intake is necessary for body function, yet balancing energy intake and total energy expenditure (TEE) to avoid inappropriate weight gain is difficult for many individuals. In 2002, the Institute of Medicine Food and Nutrition Board published the dietary reference intake (DRI) estimated energy requirements (EER), which is the energy intake needed to maintain energy balance for healthy adults by sex, age, weight, height, and physical activity level (1). These DRI estimates were calculated with equations that were based on a pooled analysis of doubly labeled water (DLW) studies, with a total of 408 normal-weight and 360 overweight and obese persons. One of the research recommendations in the report called for further data, in particular, more data on persons aged 40–60 y (1).

The DLW method is a noninvasive technique for measuring TEE in free-living individuals over a 1- to 2-wk period (2). Because of the expense and limited availability of DLW, however, few studies have measured TEE in a large cohort. The Health, Aging, and Body Composition study measured TEE with the use of DLW and compared the results with values predicted by the DRI equations in 288 black and white men and women aged 70–79 y (3). In that population, the DRI equation was found to be accurate when compared with TEE from DLW, with a mean difference of 0 ± 14%. The Observing Protein and Energy Nutrition (OPEN) Study obtained estimates of TEE with the use of DLW in 484 men and women aged 40–69 y (4). The present article reports energy expenditure from the OPEN Study, compares TEE by sex and personal characteristics, and evaluates the DRI EER equation for this population.

SUBJECTS AND METHODS

Study population

Details of the OPEN Study are described elsewhere (4). Study participants were recruited from a random sample of 5000 households in the metropolitan area of Washington, DC (Montgomery County, MD), that included a household member aged 40–69 y. Of 837 eligible participants, 614 initially agreed to participate in the study; 484 of these (261 men and 223 women) attended the first scheduled visit and were dosed with DLW. The study was

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[1] From the Division of Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, NC (JAT); the Department of Nutritional Sciences, University of Wisconsin, Madison, WI (DAS); the Applied Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD (AFS and RPT); the Biometry Research Group, Division of Cancer Prevention, National Cancer Institute, Bethesda, MD (VK); and the Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD (AS).

[2] Supported by the National Cancer Institute, Divisions of Cancer Control and Population Sciences and Cancer Epidemiology and Genetics.

[3] Address reprint requests to JA Tooze, Department of Biostatistical Sciences, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157. E-mail: jtooze@wfubmc.edu.

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Procedures

Between September 1999 and March 2000, participants in the OPEN Study completed 3 visits over a period of ≈3 mo; only 2 participants dropped out of the study. At visit 1, after fasting overnight, the participants provided informed consent, had height and weight measured, and received their first dose of DLW. The body mass index (BMI; in kg/m^2) calculated at this visit was used in all analyses. At visit 2, which was scheduled 11–14 d after visit 1, the participants completed the DLW protocol and were weighed. In addition to the main study, a small substudy was conducted to determine the between- and within-person variation in TEE. Fourteen men and 11 women in the main study were dosed with DLW a second time at visit 2 and returned 11–14 d later to complete the DLW protocol (5).

Total energy expenditure and fat-free mass measurements

Details of how the DLW studies were performed are described elsewhere (4, 5). A 5-urine specimen protocol was used, in which total body water was measured by the plateau method (6). DLW was dosed orally at ≈2 g of 10 atom percent ^{18}O labeled water and 0.12 g of 99.9 atom percent deuterium/kg of estimated total body water. TEE from DLW was calculated according to Racette et al (7) and by using the modified Weir equation, assuming a respiratory quotient of 0.86. For the 25 substudy participants, test-retest measurements of total body water and TEE were performed ≈2 wk apart. From the substudy, the within-subject CV for total body water was 1.8% and the CV for TEE was 5.1% (5). TEE measures were excluded for unacceptable internal agreement ($n = 2$), failure to isotopically equilibrate on dosing day ($n = 10$), isotopic dilution space ratios outside the range of 1.00–1.08 ($n = 6$), lack of tracer in the final urine specimen due to high water turnover ($n = 5$), or missing specimens ($n = 10$). Fat-free mass (FFM) was determined from the total body water measurement from DLW with the use of a hydration constant of 0.73. EER was calculated from the DRI equations by sex and weight status (normal weight, overweight, or obese) (1).

Resting metabolic rate and physical activity energy expenditure

Resting metabolic rate (RMR) was estimated from weight, height, and age by using the equation developed by Mifflin for adults (8):

$$\text{RMR (kcal/d) (women)} = 9.99 \times \text{weight (kg)} + 6.25 \times \text{height (cm)} - 4.92 \times \text{age (y)} + 5 \quad (1)$$

$$\text{RMR (kcal/d) (men)} = 9.99 \times \text{weight (kg)} + 6.25 \times \text{height (cm)} - 4.92 \times \text{age (y)} - 161 \quad (2)$$

We considered using the Cunningham equation (9) to estimate RMR rather than the Mifflin equation. We found the RMR values estimated by these equations to be very similar, with 89% of the RMR values estimated by Cunningham to be within 10% of the Mifflin values. Compared with the Cunningham equation, the Mifflin equation resulted in slightly higher RMR values for those in the upper tail of the distribution and slightly lower RMR values for those in the lower tail of the distribution. Physical activity energy expenditure (PAEE) was estimated from TEE and RMR, assuming the thermic effect of food was 10% of TEE:

$$\text{PAEE (kcal/d)} = 0.9 \times \text{TEE} - \text{RMR} \quad (3)$$

Physical activity level (PAL) was estimated by dividing TEE by the estimate of RMR. This estimated PAL value was categorized and used in the estimation of EER from the DRI equation.

Menopausal status

Menopausal status was determined by a questionnaire at Visit 1, which collected information on menstruation in the past 12 mo, the date of last menstrual period, and average cycle length. Women with amenorrhea for 12 mo or longer were considered postmenopausal. Women who reported a menstrual cycle in the past year were considered premenopausal. This group also includes some perimenopausal women ($n = 7$) who reported menstruation in the past 11 mo, but not the past 3 mo.

Statistical methods

Before the statistical analyses were conducted, the data were examined for outliers with the use of a cutoff of 2 times the interquartile range above or below the interquartile range upper or lower limit. Chi-square tests were used to compare the characteristics of the study participants by sex and to compare BMI category by age decade. Energy expenditure components were compared by sex and menopausal status by using t tests for unadjusted comparisons and analysis of covariance to adjust for weight and height or fat-free mass. Differences in energy expenditure by demographic characteristics were compared stratified by sex for two-level variables using t tests and analysis of variance for variables with >2 levels. The Tukey-Kramer method was used for multiple pairwise comparisons. The effects of age and BMI on TEE were further explored by using general linear models with sex and the variable of interest (age or BMI) and their interaction as predictor variables; some analyses included FFM and both age and BMI. We used an F test to test for a linear trend of age or BMI on TEE with the use of the median value for each category. If this test was significant, we then compared this model with one with the continuous variable as a predictor and chose the model with the smallest mean square error. TEE from DLW was compared with the EER from the DRI equation by calculating the percentage difference in TEE by the 2 methods. Linear regression on the natural log scale (to ensure homoscedasticity) was used to assess the correlation between the prediction of TEE from the DRI equation and the DLW value and to determine whether the relation differed from the line of identity. All analyses were done in SAS (version 9.1; SAS Institute Inc, Cary, NC). All statistical tests were two-sided at an α-level of 0.05 unless otherwise noted.

RESULTS

Of the 484 participants who completed the DLW protocol, TEE information was unusable from 33 participants in the main study and 1 participant in the substudy, which resulted in a final sample size of 451 participants, with repeat measures of DLW for 24 participants. No outliers were found. The demographic characteristics of the participants are presented in **Table 1**. Slightly

TABLE 1
Characteristics of the study population

	Women (n = 206)	Men (n = 244)
	n (%)	
Age (y)		
40–49	80 (39)	90 (37)
50–59	77 (37)	81 (33)
60–69	49 (24)	73 (30)
Race[1]		
Non-Hispanic white	159 (77)	211 (86)
Other or unknown	47 (23)	33 (14)
Smoking status		
Current	27 (13)	21 (9)
Former	55 (27)	83 (34)
Never	123 (60)	140 (57)
Education level[1]		
High school or less	40 (19)	20 (8)
Some college	52 (25)	49 (20)
College graduate	58 (28)	84 (34)
Postgraduate	51 (25)	90 (37)
BMI (kg/m^2)[1]		
<25.0	79 (38)	60 (25)
25.0–29.9	67 (33)	115 (47)
>29.9	60 (29)	69 (28)

[1] Women differed significantly from men by chi-square test ($P < 0.05$).

TABLE 2
Energy expenditure components[1]

	Women (n = 206)	Men (n = 244)	P[2]
TEE (kcal/d)[3]	2308 ± 33	2899 ± 30	<0.0001
FFM (kg)[3]	42.4 ± 0.5	58.6 ± 0.5	<0.0001
TEE$_{\text{weight,height}}$ (kcal/d)[4]	2501 ± 32	2737 ± 28	<0.0001
TEE$_{\text{FFM}}$ (kcal/d)[5]	2727 ± 28	2545 ± 25	<0.0001
RMR (kcal/d)[6]	1328 ± 13	1716 ± 12	<0.0001
PAL	1.75 ± 0.016	1.69 ± 0.014	0.0051
PAEE (kcal/d)[7]	750 ± 23	893 ± 21	<0.0001
PAEE$_{\text{weight,height}}$ (kcal/d)[4]	794 ± 27	855 ± 24	0.1540
PAEE$_{\text{FFM}}$ (kcal/d)[5]	929 ± 26	741 ± 23	<0.0001

[1] All values are $\bar{x}$ ± SEM. TEE, total energy expenditure; FFM, fat-free mass; RMR, resting metabolic rate; PAL, physical activity level; PAEE, physical activity energy expenditure.

[2] P value from t test.

[3] From doubly labeled water.

[4] Adjusted for weight and height.

[5] Adjusted for fat-free mass.

[6] Estimated by using the Mifflin equation: RMR (F): 9.99 × weight (kg) + 6.25 × height (cm) − 4.92 × age (y) + 5; RMR (M) = 9.99 × weight (kg) + 6.25 × height (cm) − 4.92 × age (y) − 161.

[7] PAEE = TEE × 0.9 − RMR.

more than one-half of the participants were male, with approximately one-third of the participants from each age decade represented in the study. The mean age of the subjects was 52.8 y for women and 54.0 y for men. Most of the participants (82%) were non-Hispanic whites and were college graduates. Thirty-eight percent of the women and 25% of the men had BMIs <25; 29% of the sample was obese (BMI > 29.9). For women, mean weight and height were 73.2 kg and 1.63 m, respectively; for men, these values were 87.5 kg and 1.76 m, respectively. BMI did not differ significantly by age decade for women; however, significantly fewer 40–49-y-old men were obese than were men aged ≥50 y (P = 0.01).

Average TEE differed significantly between men and women (**Table 2**), with men expending more energy than did women. Although the difference decreased by 60% after adjustment for weight and height, TEE remained higher for men than for women. However, adjustment for FFM resulted in higher energy expenditure for women than for men. Average estimated PAEE was significantly higher in men than in women; this difference decreased by 57% after adjustment for weight and height and was no longer significant. After adjustment for FFM, estimated PAEE was significantly higher in women than in men. To explore these differences further, we fit a model with TEE as the outcome and adjusted for FFM and estimated PAEE. After these adjustments, there were no longer any significant differences between men and women. The average estimated PAL was also significantly higher in women than in men.

We found few differences in energy expenditure among women by menopausal status (**Table 3**). TEE did not differ significantly by menopausal status. Postmenopausal women had significantly higher BMI values on average than did premenopausal women ($P < 0.05$). When TEE was adjusted for weight and height, premenopausal women had a significantly higher average TEE than did postmenopausal women (91 kcal/d, $P <$ 0.05). However, when TEE was adjusted for FFM, which itself did not differ significantly between premenopausal and postmenopausal women, there was no significant difference in TEE by menopausal status.

TABLE 3
Energy expenditure components by menopausal status[1]

	Premenopausal[2] (n = 90)	Postmenopausal (n = 110)	P[3]
TEE (kcal/d)[4]	2327 ± 39	2290 ± 40	0.5238
BMI (kg/m^2)	26.5 ± 0.6	28.4 ± 0.6	0.0205
FFM (kg)[4]	42.5 ± 0.7	42.1 ± 0.6	0.6547
FFM$_{\text{FM,height}}$ (kg)[5]	43.3 ± 0.4	41.5 ± 0.4	0.0015
TEE$_{\text{weight,height}}$ (kcal/d)[6]	2356 ± 32	2265 ± 29	0.0353
TEE$_{\text{FFM}}$ (kcal/d)[7]	2315 ± 28	2298 ± 26	0.6496
RMR (kcal/d)[8]	1334 ± 19	1317 ± 18	0.5170
PAL	1.75 ± 0.02	1.74 ± 0.02	0.8386
PAEE (kcal/d)[9]	759 ± 27	744 ± 26	0.6954
PAEE$_{\text{weight,height}}$ (kcal/d)[6]	765 ± 28	739 ± 25	0.4889
PAEE$_{\text{FFM}}$ (kcal/d)[7]	756 ± 27	747 ± 24	0.7991

[1] All values are $\bar{x}$ ± SEM. TEE, total energy expenditure; FFM, fat-free mass; FM, fat mass; RMR, resting metabolic rate; PAL, physical activity level; PAEE, physical activity energy expenditure.

[2] Premenopausal status: menstrual period in previous 11 mo, also includes some women (n = 7) of perimenopausal status with no menses in previous 3 mo, but menses in past 11 mo; postmenopausal status: ≥12 mo of amenorrhea.

[3] P from t test for unadjusted comparisons and analysis of covariance for adjusted comparisons.

[4] From doubly labeled water.

[5] Adjusted for fat mass and height.

[6] Adjusted for weight and height.

[7] Adjusted for fat-free mass.

[8] Estimated by using the Mifflin equation: RMR (F): 9.99 × weight (kg) + 6.25 × height (cm) − 4.92 × age (y) + 5; RMR (M) = 9.99 × weight (kg) + 6.25 × height (cm) − 4.92 × age (y) − 161.

[9] PAEE = TEE × 0.9 − RMR.

TABLE 4

Total energy expenditure by demographic characteristics stratified by sex[1]

	Women (n = 206)	Men (n = 244)
	kcal/d	
Age (y)[2]		
40–49	2410 ± 46	3007 ± 59
50–59	2281 ± 46	2944 ± 55
60–69	2186 ± 42	2715 ± 56
BMI (kg/m^2)[3]		
<25.0	2118 ± 36	2626 ± 45
25.0–29.9	2284 ± 38	2823 ± 42
30.0–34.9	2505 ± 62	3152 ± 60
>34.9	2728 ± 90	3576 ± 196
Race		
Non-Hispanic white	2321 ± 31	2911 ± 36
Other or unknown	2268 ± 60	2820 ± 97
Smoking status		
Current	2266 ± 74	3122 ± 171
Former	2274 ± 48	2918 ± 60
Never	2332 ± 37	2854 ± 39
Education level		
High school or less	2355 ± 67	3160 ± 18
Some college	2269 ± 49	2943 ± 79
College graduate	2293 ± 46	2871 ± 54
Postgraduate	2312 ± 62	2849 ± 49

[1] All values are $\bar{x}$ ± SEM.

[2] Overall $P < 0.01$ by ANOVA; for women and men, age group 40–49 y was significantly different from age group 60–69 y ($P < 0.05$). For men, age group 50–59 y was significantly different from age group 60–69 y ($P < 0.05$). The Tukey-Kramer method was used to adjust for multiple comparisons.

[3] Overall $P < 0.0001$ by ANOVA; for women and men, all pairwise comparisons of BMI categories were significantly different after using the Tukey-Kramer method to adjust for multiple comparisons.

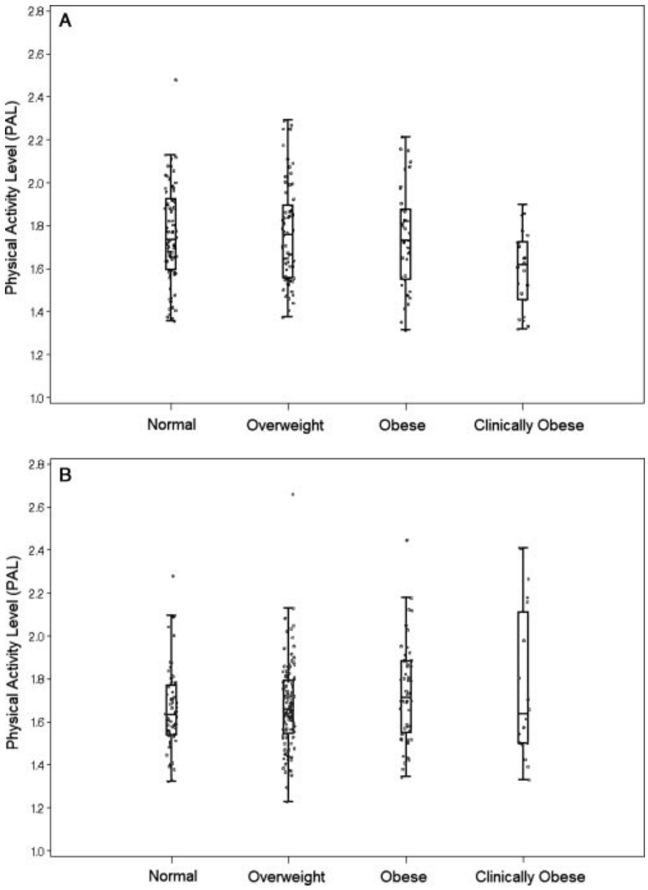

FIGURE 1. Physical activity level (PAL) by BMI classifications in women (A) and in men (B). There was a significant interaction between sex and BMI classification ($P = 0.02$) in a two-way ANOVA model.

TEE by demographic characteristics stratified by sex is shown in **Table 4**. TEE differed significantly by age decade, with adults in the seventh decade (ages 60–69 y) having the lowest TEE. Using age as a continuous variable was superior to using age categories. TEE was linearly negatively associated with age; the relation between TEE and age did not differ by sex ($P = 0.33$). The mean (±SE) estimated slope for age was −13 ± 3 kcal/y. When we adjusted for FFM in this model, however, the estimated rate of change with age became significantly different by sex ($P = 0.02$), with a nonsignificant decrease of 3 ± 3 kcal/y for women and a statistically significant decrease of 11 ± 2 kcal/y for men.

BMI as a continuous variable to predict TEE was superior to using categories of BMI. TEE increased linearly with BMI, with significantly different ($P = 0.0002$) rates of change for men and women. The rate of increase was 63 ± 6 kcal·kg^{-1}·m^{-2} for men and 36 ± 5 kcal·kg^{-1}·m^{-2} for women. The relation between estimated PAL and BMI group differed by sex ($P = 0.02$). Specifically, normal and overweight women had a higher estimated PAL than did obese and clinically obese women; this relation was not observed for men. Estimated PAL by BMI group stratified by sex is illustrated in **Figure 1**.

The accuracy of the DRI prediction equation was assessed by *1*) comparing the individual-level prediction of TEE with the value of TEE from DLW (**Figure 2**) and *2*) regressing TEE from DLW on TEE from the DRI equation. TEE from DLW was lower than TEE estimated from the DRI equation, with a mean difference of −122 ± 13 kcal/d for women and −199 ± 15 kcal/d for men. The average percentage difference was −5.9 ± 0.6% for women and −7.5 ± 0.5% for men. Sixty-eight percent of the men and 64% of the women had predicted DRI TEE values within 10% of the DLW value. The relative percentage difference between the DRI equation and the DLW measure was not significantly different by BMI category (normal, overweight, obese, clinically obese) for men ($P = 0.83$) but was significantly different for women ($P = 0.02$), with clinically obese women having the largest deviation on average (−10.8 ± 1.7%). As is illustrated in **Figure 3**, TEE from the DRI equation was highly correlated with TEE from DLW ($r = 0.93$). The slope for the relation between TEE from the DRI equation and TEE from DLW (both on the natural log scale) did not differ by sex ($P = 0.82$). Although the intercept was different by sex ($P = 0.04$), with men having a slightly lower intercept (≈47 kcal/d on the back-transformed scale), neither intercept was significantly different from 0. The slope was not significantly different from 1 (slope = 1.01; 95% CI: 0.97, 1.06).

DISCUSSION

In this large DLW study of middle-aged men and women, the average TEE for women was lower than that for men (by 591 kcal/d). We considered differences in body composition and

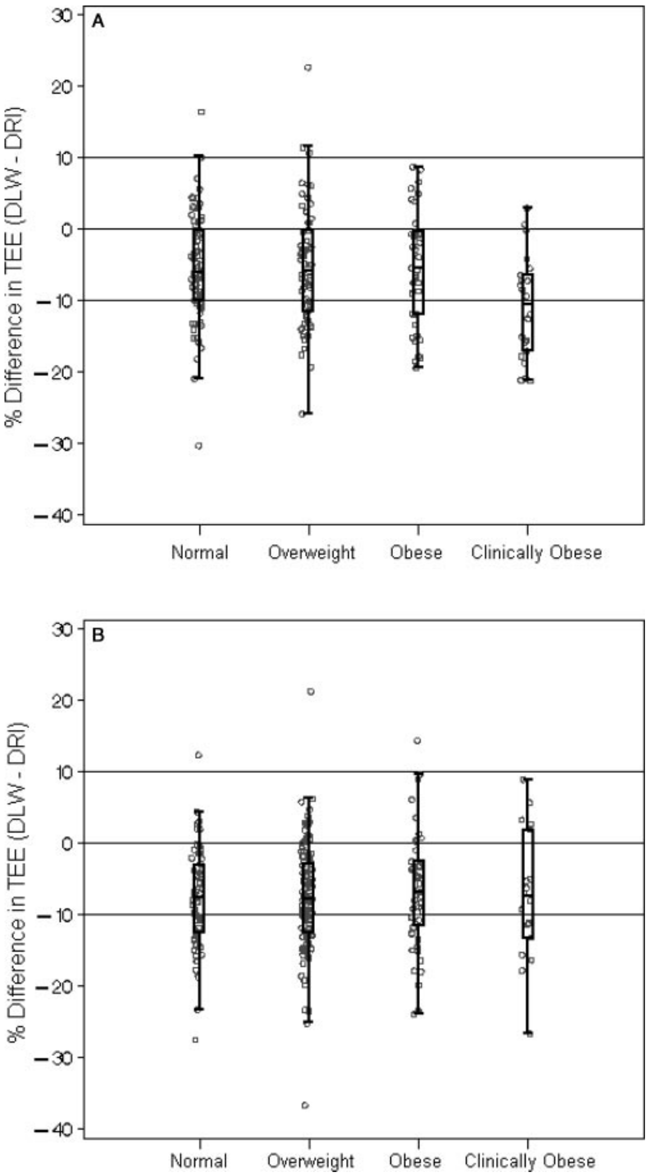

FIGURE 2. (A) Relative percentage difference in total energy expenditure (TEE) estimated from doubly labeled water (DLW) compared with TEE from the Dietary Reference Intake (DRI) equation by BMI category in women. The relative percentage difference in TEE was significantly different by BMI category ($P = 0.02$) by ANOVA. (B) Relative percentage difference in TEE estimated from DLW compared with TEE from the DRI equation by BMI category in men. The relative percentage difference in TEE was not significantly different by BMI category ($P = 0.83$) by ANOVA.

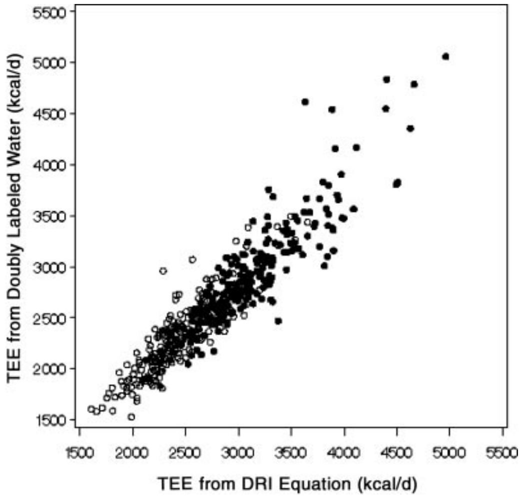

FIGURE 3. Total energy expenditure (TEE) from doubly labeled water versus predicted TEE from the Dietary Reference Intake (DRI) equation in women (○) and men (●). Pearson $r = 0.93$, $P < 0.0001$. The slope did not differ by sex ($P = 0.82$), but the intercepts were significantly different ($P = 0.04$) in a regression model.

menopausal status as possible explanations for this difference and concluded that the difference was primarily due to differences in FFM and estimated PAEE between men and women. The magnitude of the difference in TEE diminished with adjustment for height and weight, but TEE remained significantly higher in men (by 236 kcal/d). However, after adjustment for FFM, the subject characteristic that most highly correlates with TEE (1), the direction of the differences changed, and TEE became significantly higher in women (by 182 kcal/d). Furthermore, we did not find any significant differences in TEE by menopausal status in women. TEE was significantly higher in women than in men (by 148 kcal/d, $P < 0.05$) when adjusted for menopausal status, FFM, and age.

The difference in TEE between men and women appears to be due to greater estimated PAEE for women, which showed the same trend as TEE. The unadjusted average estimated PAEE was higher in men than in women (143 kcal/d); this difference was still significant, but smaller (61 kcal/d), when adjusted for height and weight, and reversed when adjusted for FFM (women 188 kcal/d greater than men). Similarly, estimated PAL values were higher for women than for men. When TEE was adjusted for estimated PAL in addition to menopausal status, FFM, and age, the difference in TEE between men and women was no longer statistically significant ($P = 0.30$), which indicates that differences between men and women were due to higher estimated PAL in the women. This finding is in contrast with other DLW studies that found lower TEE in women after adjustment for FFM as well as lower PAEE (3, 10). However, the women in the present study were younger and had higher mean fat mass than did the women in the other studies. The mean PAL for women in the present study was also higher than the PAL reported in the DRI report (1.75 compared with 1.69); the mean PAL for men was somewhat lower (1.69 compared with 1.72) (1). This may indicate that the women in the present study were more active, and the men possibly less active, than in the other DLW studies. However, because RMR was estimated and not measured, some of the differences may also have been due to errors in estimating RMR.

Our results corroborate the DRI equations for total energy intake (1). Although we found the equation to slightly overestimate TEE for this age group, particularly for clinically obese women, TEE from DLW and the DRI equation were highly correlated. In addition, the relation between TEE from DLW and TEE from the DRI equation did not differ from the line of identity. According to the results of this analysis, the estimated EER for clinically obese women appears to be too high by ≈10%. Dietitians and others advising clinically obese women on weight loss should be aware of this potential limitation. It is also important to note that this analysis was intended to validate the DRI equation by using an independent DLW sample. The equation was validated in terms of its intended use to estimate the EER of a healthy adult of a specified age, sex, weight, height, and physical activity level. We did not validate the equation for use in nutritional epidemiology or surveillance studies. Furthermore, it is unclear how one uses the equation without a good estimate of PAL, which limits its general use.

TEE was negatively associated with age in both men and women, with 40–49-y-olds having a higher average TEE than did 60–69-y-olds, even though mean BMI was greater in 60–69-y-old men. When adjusted for FFM, this difference became nonsignificant for women, which indicates that changes in body composition in the seventh decade may explain part of the decrease in energy needs for women. Adjustment for FFM did not change the relation for men.

TEE was found to be linearly related to BMI in this population, with different slopes for men and women. A 5-unit change in BMI corresponded to a 179-kcal/d change in TEE (95% CI: 134, 225 kcal/d) for women and a 315-kcal/d change (95% CI: 259, 371 kcal/d) for men. Our results agree with other studies (11) that support increasing energy expenditure with increasing BMI, even though self-reported energy intake is consistently low in obese individuals (12). Weight and BMI were highly correlated with the TEE adjusted for estimated PAEE (attributable primarily to RMR), but not with the component related to PAEE.

Although this was a large DLW study of middle-aged men and women, it does have some limitations. First, RMR was not measured and had to be estimated, which introduces error. Second, the OPEN Study population is not representative of the US population. Specifically, the participants were primarily well-educated non-Hispanic whites, and the study did not include any participants under 40 or over 69 y age. The proportion of participants who were overweight (40%) or obese (29%) was higher than in the concurrent US population. It is important to note that the population used to develop the DRI equation also was not representative of the US population, and therefore the current EER are not based on a representative sample. Additionally, this was a cross-sectional analysis of TEE and personal characteristics, and the results should be interpreted in light of this.

This large DLW study supports the use of the DRI equation for EER in middle-aged adults. We also found that energy expenditure was lower in the seventh decade of life, which could have been due to changes in body composition in women. Furthermore, we found that when TEE was adjusted for FFM, TEE in middle-aged women was not lower but rather higher than in men, which appeared to be due to higher levels of physical activity.

The contributions of the authors were as follows—JAT: conception of the study, design of the analysis, data analysis, data interpretation, and manuscript preparation; RPT: conception of the study, conception and conduct of the OPEN Study, data interpretation, and manuscript preparation; DAS: conception of the study, analysis of doubly labeled water data, data interpretation, and manuscript preparation; AFS and AS: conception and conduct of the OPEN Study, data interpretation, and manuscript preparation; and VK: data interpretation and manuscript preparation. None of the authors had any financial or personal conflicts of interest with the research sponsor.

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