Physical activity and gain in abdominal adiposity and body weight: prospective cohort study in 288,498 men and women[1–4]

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ABSTRACT

Background: The protective effect of physical activity (PA) on abdominal adiposity is unclear.

Objective: We examined whether PA independently predicted gains in body weight and abdominal adiposity.

Design: In a prospective cohort study [the EPIC (European Prospective Investigation into Cancer and Nutrition)], we followed 84,511 men and 203,987 women for 5.1 y. PA was assessed by a validated questionnaire, and individuals were categorized into 4 groups (inactive, moderately inactive, moderately active, and active). Body weight and waist circumference were measured at baseline and self-reported at follow-up. We used multilevel mixed-effects linear regression models and stratified our analyses by sex with adjustments for age, smoking status, alcohol consumption, educational level, total energy intake, duration of follow-up, baseline body weight, change in body weight, and waist circumference (when applicable).

Results: PA significantly predicted a lower waist circumference (in cm) in men (β = −0.045; 95% CI: −0.057, −0.034) and in women (β = −0.035; 95% CI: −0.056, −0.015) independent of baseline body weight, baseline waist circumference, and other confounding factors. The magnitude of associations was materially unchanged after adjustment for change in body weight. PA was not significantly associated with annual weight gain (in kg) in men (β = −0.008; 95% CI: −0.02, 0.003) and women (β = −0.01; 95% CI: −0.02, 0.0006). The odds of becoming obese were reduced by 7% ($P < 0.001$) and 10% ($P < 0.001$) for a one-category difference in baseline PA in men and women, respectively.

Conclusion: Our results suggest that a higher level of PA reduces abdominal adiposity independent of baseline and changes in body weight and is thus a useful strategy for preventing chronic diseases and premature deaths. *Am J Clin Nutr* 2011;93:826–35.

INTRODUCTION

More than 200 million European men and women are either overweight or obese; of these ≈70 million individuals are obese (1). The geographical variation in obesity prevalence within Europe is substantial, with higher prevalence values observed in southern and eastern compared with western and northern parts (2). This variation indicates that genetic, cultural, environmental, and socioeconomic factors contribute to the obesity epidemic. Although several common genetic variants that contribute to excessive body weight and obesity have been identified (3–5), it is likely that the main contributor to the recent obesity epidemic is caused by an imbalance between energy intake and energy expenditure.

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Abdominal obesity, which is usually measured as the waist circumference or waist-to-hip ratio, is associated with chronic diseases and premature deaths independent of body mass index (BMI; in kg/m^2) and appears to be a stronger predictor of morbidity and mortality compared with BMI (6–8).

Low levels of physical activity are assumed to be associated with obesity. However, physical activity only weakly predicts gain in body weight and BMI (9, 10) and the preventive effect of physical activity may be restricted to those who are of normal weight at baseline (11). To our knowledge, whether physical activity predicts a gain in abdominal obesity and whether this association is independent of the baseline and concomitant change in body weight is unknown. Understanding the independent associations between physical activity and gains in abdominal adiposity and body weight is important for preventive purposes when implementing physical activity as a population health strategy against obesity and its comorbidities.

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Therefore, we examined whether physical activity predicted *1*) a gain in body weight, *2*) a gain in waist circumference independent of the baseline body weight and concomitant change in body weight, and *3*) the development of obesity in individuals who were nonobese at baseline. We used data from the European Prospective Investigation into Cancer and Nutrition (EPIC)–Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating Out of Home and Obesity (PANACEA) study, which is a large, well-characterized cohort study that includes a total of 288,498 European men and women.

SUBJECTS AND METHODS

Study population

The EPIC study is an ongoing prospective cohort study that includes 521,448 men and women from 23 centers in 10 European countries (Denmark, France, Germany, Greece, Italy, Netherlands, Norway, Spain, Sweden, and the United Kingdom) who were between 25 and 79 y of age at enrollment. Because of differences in assessments of main outcomes (self-report compared with direct measurement) between centers in the Netherlands and the United Kingdom, these centers were split into 2 (Utrecht and Doetinchen/Amsterdam) and 3 (Cambridge, UK Health conscious, and UK General) study locations, respectively, which made a total of 28 study locations in the EPIC–PANACEA study.

Participants were mainly recruited from the general population in a given geographical area (city, county, or province) in each center. From the 521,448 men and women initially recruited, we excluded participants (n = 23,479) according to the EPIC–PANACEA protocol exclusion criteria [ie, no recorded length of follow-up, no data on dietary intake, an extreme ratio of energy intake to estimated energy requirement (12), no data on smoking, alcohol consumption, and education level, pregnant women, and extreme data on anthropometric measures as previously described (13)]. Of the remaining 497,969 participants, follow-up data on body weight was not available in 121,853 men and women. Furthermore, 2066 individuals were excluded because of extreme anthropometric measures at follow-up (ie, body weight >250 kg, BMI <16, and an annual average weight change less than −5 kg/y or greater than +5 kg/y). Information on physical activity were not available for 43,320 participants, mainly from Tromsö, Norway, and Umeå, Sweden, because the questionnaire used to assess physical activity in these cohorts differed from the core EPIC questionnaire used in the other cohorts and was not compatible. A total of 27,306 individuals were further excluded because of history of heart disease, cancer, diabetes, or stroke at baseline. Finally, we excluded all participants without available information on BMI at either baseline or follow-up or other missing covariates (n = 14,926), which left 288,498 participants (84,511 men and 203,987 women) for the current analyses. Individuals without follow-up data were 0.1 y older, 0.6 kg heavier, 0.6 cm taller, had a 0.5 higher BMI, and reported lower levels of physical activity (59.5% compared with 55.9% were categorized as inactive or moderately inactive in individuals with and without follow-up data).

A total of 32,143 men and 48,061 women from 5 study locations (Denmark, Italy, Potsdam, Germany, Doetinchem, Netherlands, and Cambridge, United Kingdom) also provided data on waist circumferences at baseline and follow-up.

All participants provided written informed consent to participate in the study. Approval for the study was obtained from the ethical review boards of the International Agency for Research on Cancer and from all local institutions in which participants had been recruited for the EPIC study.

Anthropometric measures

Baseline body weights (kg) and heights (cm) were measured according to standardized procedures without shoes (14) except for at the centers of Oxford (United Kingdom), France, and Norway where self-reported anthropometric values at baseline were used. Baseline waist circumferences (cm) were measured either at the narrowest torso circumference or at the midpoint between the lower ribs and iliac crest. Weight and waist measurements were corrected to account for protocol differences between centers as previously described (14). At follow-up, body weights and waist circumferences were self-reported in all centers except in Cambridge (United Kingdom) and Doetinchem (Netherlands) where they were measured according to the baseline protocol. BMI was calculated as body weight (kg) divided by height squared (m^2). Individuals were categorized into normal-weight (BMI <25), overweight (BMI of 25–29.99) and obese (BMI ≥30) groups.

Physical activity

Physical activity was assessed by a validated self-report questionnaire (15, 16). Briefly, the overall physical activity was assessed from 3 questions referring to the past year. The question on occupational activity was categorized into 4 categories as follows: sedentary occupation, standing occupation (eg, hairdresser, shop assistant, or guard), manual occupation (eg, plumber, cleaner, or nurse), and heavy manual work (eg, construction worker or bricklayer). The 2 other questions asked about the duration of recreational physical activity (ie, cycling and other physical exercise such as keeping fit, jogging, or swimming). The average time spent in recreational activity per day was estimated as the mean of the self-reported total hours per week during winter and summer divided by 7. A physical activity index was derived by allocating individuals into 4 ordered categories of overall activity (inactive, moderately inactive, moderately active, and active) as previously described (16). We examined the validity of the derived 4-category physical activity index in 1941 participants who were similar in age and sex as the original EPIC cohort from 10 of the EPIC countries by using the combined movement and heart-rate sensing as our criterion (17, 18). The physical activity energy expenditure (PAEE) increased significantly by increasing categories of self-reported physical activity (P for trend < 0.0001), and a significant correlation between measured PAEE and the categorical self-reported physical activity index was observed in all countries (Spearman's correlation = 0.17–0.37, $P < 0.01$) (PH Peeters, NJ Wareham, and U Ekelund, personal communication, 2 November 2010). Furthermore, this index was previously shown to predict all-cause and cardiovascular mortality (19).

Assessment of covariates

Dietary intakes at baseline were measured by using country-specific validated food-frequency questionnaires. Most centers adopted a self-administered dietary questionnaire of 88–266 food items (20). Nutrient intakes were calculated by using the EPIC nutrient database, which is a standardized food-composition table (20), and daily total energy intake was estimated in each individual in kilocalories.

Standard questionnaires were used at baseline to collect information on participant sociodemographic characteristics and lifestyle variables such as smoking status (never smoker, former smoker, and current smoker), educational level (according to the maximum achieved school level as follows: none, primary school, technical school, secondary school, and university degree), and alcohol consumption at recruitment in a 6-level variable for women (0, >0 to ≤6, 7–18, 19–30, 31–60, and >60 g alcohol/d) and a 7-level variable for men (0, >0 to ≤6, 7–18, 19–30, 31–60, 61–96, and >96 g alcohol/d).

Statistical analyses

Characteristics of the study population were summarized separately for men and women by using means and SDs for continuous variables and frequencies and percentages for categorical variables. All described analyses were performed separately in men and women.

Linear regression was used to estimate the location-specific associations between physical activity (as a continuous variable with 4 levels) and annual change in *1*) body weight and *2*) waist circumference. Random intercepts and slopes were included when there was more than one study location in a particular study center. The models were adjusted for baseline weight, baseline waist circumference (when the annual change in waist circumference was the outcome), age at recruitment, smoking, alcohol consumption, education, total energy intake, and duration of follow-up. To examine whether physical activity predicted a change in waist circumference independent of a change in body weight, we reanalyzed our data by substituting the baseline body weight with the change in body weight between baseline and follow-up.

A 3-level (level 1: individuals; level 2: centers; and level 3: country) mixed-effects linear regression model was used to estimate the overall associations between physical activity and annual change in *1*) body weight and *2*) waist circumference. The same covariates listed above [baseline weight, baseline waist circumference (when the annual change in waist circumference was the outcome), age at recruitment, smoking, alcohol consumption, education, total energy intake, and duration of follow-up were included in the models as fixed effects]. The interactions between physical activity and age and location were tested. The described modeling approaches were also used to estimate location-specific and overall associations within subgroups defined by age (<50 and ≥50 y of age) and BMI groups (normal weight, overweight, and obese). Additional analyses were performed in similar models in which physical activity was modeled as a categorical variable with 4 categories [inactive (reference), moderately inactive, moderately active, and active) to test for differences between the reference category and the 3 other categories.

Location-specific estimates of the odds ratio of becoming obese per one-level difference in physical activity (eg, inactive compared with moderately inactive) in nonobese individuals were estimated by using logistic regression adjusted for the same set of confounders listed previously. Odds ratios from each location

TABLE 1
Descriptive characteristics of participants stratified according to baseline overall physical activity[1]

	Inactive	Moderately inactive	Moderately active	Active
Men (*n* = 84,511)				
n	14,683	26,590	21,573	21,665
Age (y)	56.1 ± 9.7[2]	53.1 ± 8.9	52.0 ± 8.7	51.3 ± 8.7
Height (cm)	173.2 ± 7.5	174.9 ± 7.2	174.5 ± 7.4	175.1 ± 7.2
Weight (kg)	81.5 ± 12.4	81.2 ± 11.6	80.9 ± 11.4	80.9 ± 11.3
BMI (kg/m^2)	27.2 ± 3.8	26.6 ± 3.5	26.6 ± 3.5	26.4 ± 3.4
Waist circumference (cm)	97.3 ± 10.4	95.1 ± 9.8	94.4 ± 9.7	93.4 ± 9.7
Energy intake (kcal/d)	2347 ± 633	2408 ± 624	2494 ± 651	2587 ± 671
Annual weight change (kg)	0.04 ± 1.1	0.03 ± 1.0	0.05 ± 1.0	0.05 ± 1.0
Annual waist circumference change (cm)[3]	0.43 ± 1.22	0.50 ± 1.11	0.53 ± 1.09	0.52 ± 1.10
Educational level [*n* (%)]				
None (*n* = 4651)	1315 (28.3)	1187 (25.5)	1336 (28.7)	813 (17.5)
Primary (*n* = 25,427)	4476 (17.6)	6769 (26.6)	6508 (25.6)	7674 (30.2)
Technical/professional (*n* = 20,564)	3017 (14.7)	5997 (29.2)	5310 (25.8)	6240 (30.3)
Other secondary (*n* = 8855)	1688 (19.1)	3164 (35.7)	2048 (23.1)	1955 (22.1)
Higher (*n* = 25,014)	4187 (16.7)	9473 (37.9)	6371 (25.5)	4983 (19.9)
Smoking status [*n* (%)]				
Never (*n* = 27,328)	4307 (15.8)	8716 (31.9)	7157 (26.2)	7148 (26.2)
Former (*n* = 31,398)	5446 (17.3)	9961 (31.7)	7903 (25.2)	8088 (25.8)
Current (*n* = 25,785)	4930 (19.1)	7913 (30.7)	6513 (25.3)	6429 (24.9)
Alcohol consumption [*n* (%)]				
0 g/d (*n* = 5240)	1472 (28.1)	1476 (28.2)	1177 (22.5)	1115 (21.3)
≤6 g/d (*n* = 15,785)	3286 (20.8)	4895 (31.0)	3739 (23.7)	3865 (24.5)
6.1–18 g/d (*n* = 24,360)	4029 (16.5)	7930 (32.6)	6160 (25.3)	6241 (25.6)
18.1–30 g/d (*n* = 14,303)	2108 (14.7)	4628 (32.4)	3880 (27.1)	3687 (25.8)
31–60 g/d (*n* = 17,250)	2570 (14.9)	5510 (31.9)	4591 (26.6)	4579 (26.5)
60.1–96 g/d (*n* = 5688)	917 (16.1)	1635 (28.7)	1518 (26.7)	1618 (28.4)
>96.1 g/d (*n* = 1885)	301 (16.0)	516 (27.4)	508 (26.9)	560 (29.7)
Women (*n* = 203,987)				
n	45,833	74,686	51,004	32,464
Age (y)	53.8 ± 9.8	51.6 ± 9.3	50.2 ± 8.6	50.5 ± 9.2
Height (cm)	159.4 ± 6.7	161.8 ± 6.4	162.6 ± 6.2	163.7 ± 6.2
Weight (kg)	67.0 ± 12.1	64.6 ± 11.2	63.6 ± 10.8	65.2 ± 10.9
BMI (kg/m^2)	26.4 ± 4.9	24.7 ± 4.2	24.1 ± 3.9	24.3 ± 3.9
Waist circumference (cm)	84.5 ± 12.1	80.1 ± 11.0	78.8 ± 10.6	78.5 ± 10.2
Energy intake (kcal/d)	1953 ± 542	1997 ± 533	2030 ± 538	2010 ± 533
Annual weight gain (kg)	0.11 ± 1.1	0.20 ± 1.0	0.24 ± 1.0	0.20 ± 1.0
Annual waist circumference gain (cm)[4]	0.80 ± 1.30	0.98 ± 1.33	1.0 ± 1.33	1.05 ± 1.42
Educational level [*n* (%)]				
None (*n* = 12,170)	7284 (59.9)	3405 (28.0)	1182 (9.7)	299 (2.5)
Primary (*n* = 49,212)	15,499 (31.5)	17,331 (35.2)	9284 (18.9)	7098 (14.4)
Technical/professional (*n* = 40,458)	6407 (15.8)	14,573 (36.0)	9754 (24.1)	9724 (24.0)
Other secondary (*n* = 50,092)	8937 (17.8)	19,423 (38.8)	14,724 (29.4)	7008 (14.0)
Higher (*n* = 52,055)	7706 (14.8)	19,954 (38.3)	16,060 (30.9)	8335 (16.0)
Smoking status [*n* (%)]				
Never (*n* = 125,000)	31,242 (25.0)	45,923 (36.7)	30,568 (24.5)	17,267 (13.8)
Former (*n* = 44,273)	7062 (16.0)	16,085 (36.3)	12,291 (27.8)	8835 (20.0)
Current (*n* = 34,714)	7529 (21.7)	12,678 (36.5)	8145 (23.5)	6362 (18.3)
Alcohol consumption [*n* (%)]				
0 g/d (*n* = 33,063)	12,875 (38.9)	11,198 (33.9)	5945 (18.0)	3054 (9.2)
≤6 g/d (*n* = 79,798)	17,450 (21.9)	29,417 (36.9)	20,170 (25.3)	12,761 (16.0)
6.1–18 g/d (*n* = 58,052)	9795 (16.9)	21,585 (37.2)	15,952 (27.5)	10,720 (18.5)
18.1–30 g/d (*n* = 18,524)	3316 (17.9)	7018 (37.9)	5047 (27.2)	3143 (17.0)
31–60 g/d (*n* = 12,911)	2077 (16.1)	4882 (37.8)	3474 (26.9)	2478 (19.2)
>60 g/d (1693)	320 (19.5)	586 (35.8)	416 (25.4)	317 (19.3)

[1] Average physical activity energy expenditures measured by the individually calibrated combined heart rate and movement sensing in an independent validation study (*n* = 1941) across categories of physical activity in men and women, respectively, were as follows: inactive (38.1 and 39.2 kJ · kg^{-1} · d^{-1}), moderately inactive (47.5 and 39.9 kJ · kg^{-1} · d^{-1}), moderately active (48.5 and 44.7 kJ · kg^{-1} · d^{-1}), and active (56.8 and 49.3 kJ · kg^{-1} · d^{-1}).

[2] Mean ± SD (all such values).

[3] *n* = 5183, 10,451, 8216, and 10,293 for inactive, moderately inactive, moderately active, and active participants, respectively.

[4] *n* = 8653, 16,948, 11,174, and 11,286 for inactive, moderately inactive, moderately active, and active participants, respectively.

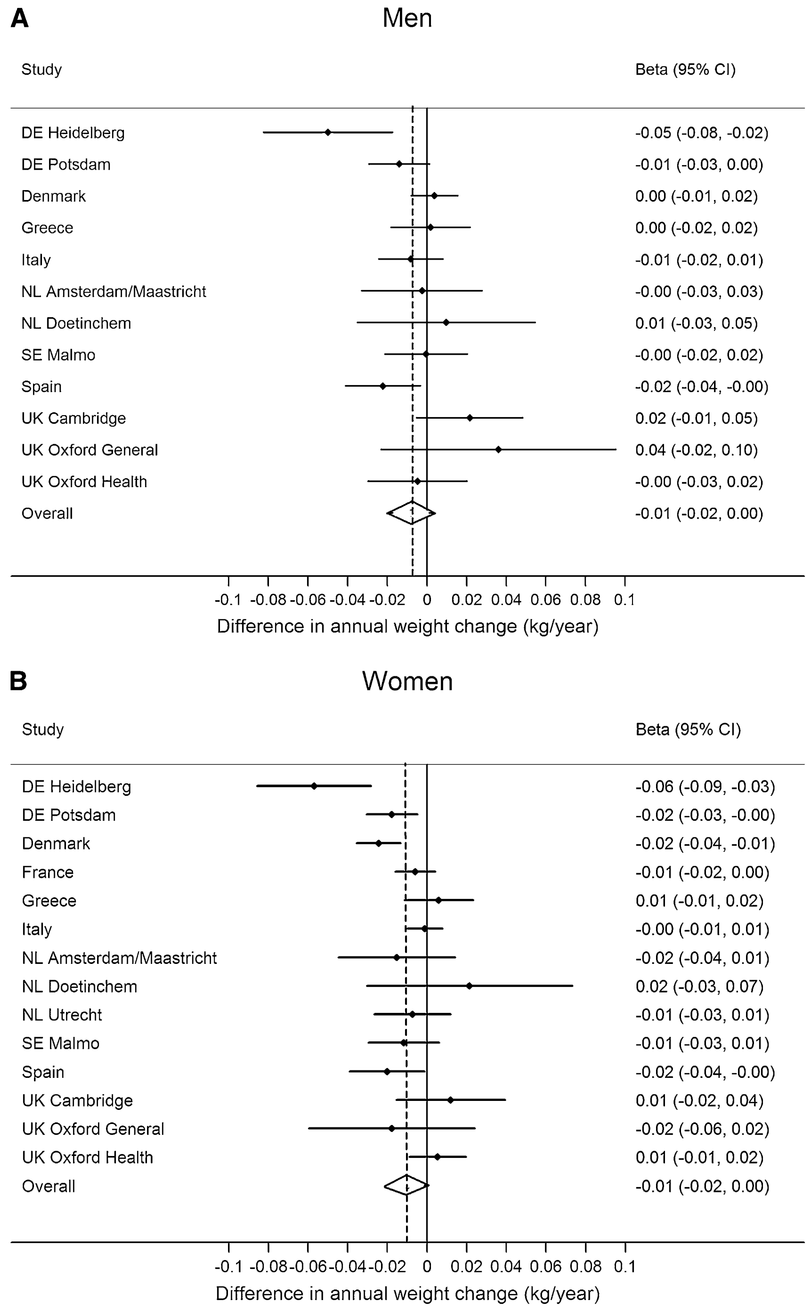

FIGURE 1. Differences in annual weight changes per one-category increment in overall physical activity in men (A) (overall $P = 0.17$, $n = 84{,}511$) and women (B) (overall $P = 0.064$, $n = 203{,}987$) after adjustment for age, baseline body weight, smoking, energy intake, alcohol consumption, educational level, and duration of follow-up. Average physical activity energy expenditures measured by the individually calibrated combined heart rate and movement sensing in an independent validation study ($n = 1941$) across categories of physical activity in men and women, respectively, were as follows: inactive (38.1 and 39.2 $kJ \cdot kg^{-1} \cdot d^{-1}$), moderately inactive (47.5 and 39.9 $kJ \cdot kg^{-1} \cdot d^{-1}$), moderately active (48.5 and 44.7 $kJ \cdot kg^{-1} \cdot d^{-1}$), and active (56.8 and 49.3 $kJ \cdot kg^{-1} \cdot d^{-1}$). DE, Germany; NL, Netherlands; SE, Sweden.

were combined to estimate an overall odds ratio by using random-effects meta-analysis. All statistical analyses were performed with Stata/SE 10.1 for Windows (StataCorp LP, College Station, TX).

RESULTS

Descriptive characteristics of participants are shown in **Table 1** and stratified by sex and level of overall physical activity at baseline. A total of 48.8% of men and 59.1% of women were categorized as inactive or moderately inactive at baseline.

Over an average (±SD) follow-up time of 5.1 ± 2.3 y, body weight increased on average by 0.48 ± 4.7 kg in men and 0.99 ± 4.5 kg in women. In men and women who provided data on waist circumferences at both the baseline and follow-up, waist circumferences increased by a mean of 3.2 ± 6.3 cm in men and 6.3 ± 7.7 cm in women.

The baseline overall physical activity was not associated with a change in body weight in men ($\beta = -0.008$; 95% CI: −0.02, 0.003; $P = 0.17$) and women ($\beta = -0.01$; 95% CI: −0.02, 0.0006; $P = 0.064$) after adjustment for age, baseline body

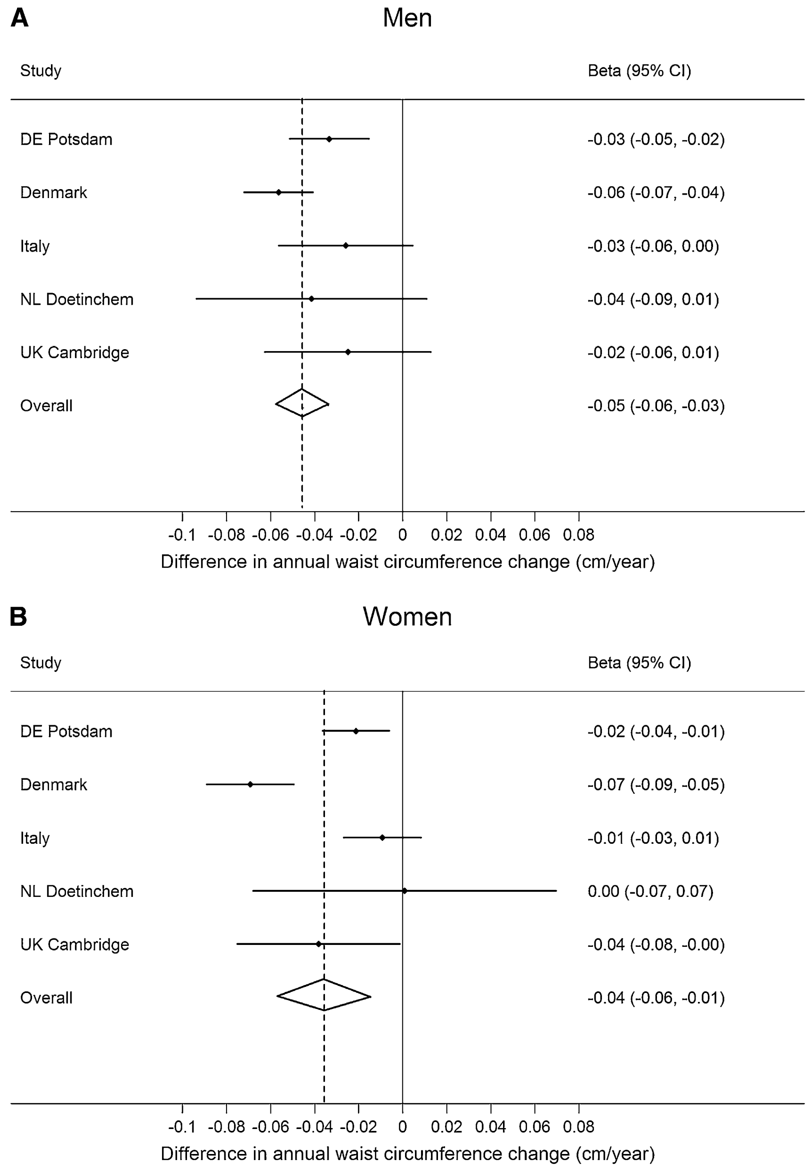

FIGURE 2. Differences in annual waist circumference changes per one-category increment in physical activity in men (A) (overall $P < 0.001$, $n = 34{,}143$) and women (B) (overall $P = 0.0008$, $n = 48{,}061$) after adjustment for age, baseline BMI, smoking, energy intake, alcohol consumption, educational level, and duration of follow-up. Average physical activity energy expenditures measured by individually calibrated combined heart rate and movement sensing in an independent validation study ($n = 1941$) across categories of physical activity in men and women, respectively, were as follows: inactive (38.1 and 39.2 kJ $\cdot$ kg^{-1} $\cdot$ d^{-1}), moderately inactive (47.5 and 39.9 kJ $\cdot$ kg^{-1} $\cdot$ d^{-1}), moderately active (48.5 and 44.7 kJ $\cdot$ kg^{-1} $\cdot$ d^{-1}), and active (56.8 and 49.3 kJ $\cdot$ kg^{-1} $\cdot$ d^{-1}). DE, Germany; NL, Netherlands.

weight, smoking, energy intake, alcohol consumption, education level, and duration of follow-up (**Figure 1**). A significant heterogeneity by age ($P < 0.001$) and study location (I^2: 47.6% and 63.0% for men and women, respectively; $P < 0.001$) was observed in both men and women. Thereafter, we performed sensitivity analyses by modeling physical activity as a categorical variable, and the results confirmed the nonsignificant association between the baseline physical activity with a change in body weight (*see* supplemental Figure 1, A–E under "Supplemental data" in the online issue).

We examined whether physical activity was associated with a change in waist circumference between baseline and follow-up after adjusting for baseline waist circumference and the same confounding factors as previously mentioned (**Figure 2**). Higher levels of baseline physical activity were significantly and inversely associated with changes in waist circumference in men ($\beta = -0.029$; 95% CI: -0.040, -0.017; $P < 0.001$) and women ($\beta = -0.035$; 95% CI: -0.056, -0.014; $P = 0.0012$). These results were materially unchanged after adjustment for baseline body weight in men ($\beta = -0.045$; 95% CI: -0.057, -0.034; $P < 0.001$) and in women ($\beta = -0.035$; 95% CI: -0.056, -0.015; $P < 0.001$), which suggested an effect of physical activity on central adiposity independent of body weight. We substituted baseline body weight with the change in body weight between baseline and follow-up as a covariate to examine whether physical activity predicted a change in waist circumference independent of a change in body weight. Higher levels of overall physical activity were significantly and inversely associated with a change in waist circumference in men ($\beta = -0.044$; 95% CI: -0.060, -0.027; $P < 0.001$) and women ($\beta = -0.027$; 95% CI:

TABLE 2

Subgroup analysis stratified by age and baseline BMI status for the prospective associations between baseline physical activity and annual change in body weight in European men and women[1]

	β Coefficient (95% CI)	P for linear trend
Men (n = 84,511)		
<50 y of age		
Normal weight (n = 10,527)	−0.025 (−0.042, −0.007)	0.006
Overweight (n = 13,756)	−0.025 (−0.058, 0.007)	0.12
Obese (n = 4217)	−0.024 (−0.064, 0.017)	0.25
All (n = 28,500)	−0.029 (−0.041, −0.016)	<0.001
≥50 y of age		
Normal weight (n = 17,966)	−0.0026 (−0.014, 0.009)	0.66
Overweight (n = 28,930)	0.0023 (−0.0083, 0.013)	0.67
Obese (n = 9115)	0.0034 (−0.022, 0.029)	0.79
All (n = 56,011)	0.00048 (−0.0074, 0.0084)	0.91
Women (n = 203,987)		
<50 y of age		
Normal weight (n = 56,832)	−0.024 (−0.032, −0.016)	<0.001
Overweight (n = 19,642)	−0.016 (−0.034, 0.0028)	0.097
Obese (n = 7835)	0.015 (−0.022, 0.053)	0.42
All (n = 84,309)	−0.015 (−0.029, −0.0007)	0.040
≥50 y of age		
Normal weight (n = 64,174)	−0.013 (−0.028, 0.002)	0.090
Overweight (n = 38,279)	−0.0028 (−0.014, 0.008)	0.62
Obese (n = 17,225)	−0.032 (−0.060, −0.004)	0.028
All (n = 119,678)	−0.012 (−0.018, −0.006)	<0.001

[1] β Coefficients and 95% CIs (kg/y) are for comparisons of effects between one category and the adjacent category for overall physical activity (eg, from inactive to moderately inactive) adjusted for baseline age, body weight, energy intake, smoking status, alcohol intake, educational level, and duration of follow-up. Data were analyzed with mixed-effects linear regression. Average physical activity energy expenditures measured by the individually calibrated combined heart rate and movement sensing in an independent validation study (n = 1941) across categories of physical activity in men and women, respectively, were as follows: inactive (38.1 and 39.2 kJ · kg^{-1} · d^{-1}), moderately inactive (47.5 and 39.9 kJ · kg^{-1} · d^{-1}), moderately active (48.5 and 44.7 kJ · kg^{-1} · d^{-1}), and active (56.8 and 49.3 kJ · kg^{-1} · d^{-1}).

−0.047, −0.0006; P = 0.011). Subsequent sensitivity analyses that modeled physical activity as a categorical variable confirmed the linear dose-response association between physical activity and a change in waist circumference (*see* supplemental Figure 2, A–E under "Supplemental data" in the online issue).

In subgroup analyses stratified by age (<50 and ≥50 y of age) and obesity status (normal weight, overweight, and obese), a higher overall physical activity predicted a lower gain in body weight in younger men and women. However, this association was mainly driven by significant associations in normal-weight individuals. In older men, physical activity was not associated with a change in body weight. In older women, higher levels of physical activity were associated with lower annual weight gains, and this association was mainly explained by an inverse association in the obese women (**Table 2**). Thereafter, we analyzed the subgroup data (stratified by age group and obesity status) by modeling physical activity as a categorical variable, and the results were remarkably similar (*see* supplemental Table 1 under "Supplemental data" in the online issue).

Prospective associations between the baseline overall physical activity and annual change in waist circumference in men and women stratified by obesity status are shown in **Table 3** (no significant heterogeneity by age was observed). Lower levels of overall physical activity consistently and significantly predicted annual changes in waist circumference across BMI groups in men and women. These associations were independent of the baseline and change in body weight, and the magnitude of associations was remarkably similar across BMI groups (Table 3). Thereafter, we analyzed the subgroup data (stratified by obesity status) by modeling physical activity as a categorical variable, and the results were confirmed (*see* supplemental Table 2 under "Supplemental data" in the online issue). To account for differences in methods between study locations we performed sensitivity analyses for the associations between the baseline physical activity with gains in body weight and waist circumference by excluding centers with self-reported measures, and the results were materially unchanged.

Of those 71,179 men and 178,927 women categorized as normal-weight or overweight (BMI <30) at baseline, 3603 (5.1%) men and 7484 (4.2%) women progressed to obesity (BMI ≥30) during 5.1 y of follow-up. The odds of becoming obese were reduced by 7% (P < 0.001) and 10% (P < 0.001) for a one-category difference in baseline physical activity in men and women, respectively (**Figure 3**).

DISCUSSION

Low levels of physical activity consistently and independently predicted gains in abdominal adiposity in normal-weight, overweight, and obese men and women. However, the prospective association between physical activity and a gain in body weight may be restricted to individuals who are younger (<50 y of age) and of normal-weight at baseline. In nonobese individuals, the

TABLE 3
Subgroup analysis stratified by baseline BMI status for the prospective associations between baseline physical activity and annual change in waist circumference in European men and women[1]

	β Coefficient (95% CI)	P for linear trend
Men		
Normal weight (n = 12,439)	−0.044 (−0.062, −0.026)	<0.001
Overweight (n = 17,406)	−0.047 (−0.062, −0.031)	<0.001
Obese (n = 4298)	−0.047 (−0.084, −0.009)	0.015
All (n = 34,143)	−0.045 (−0.057, −0.034)	<0.001
Women		
Normal weight (n = 25,740)	−0.034 (−0.062, −0.006)	0.018
Overweight (n = 16,215)	−0.040 (−0.061, −0.019)	0.0002
Obese (n = 6106)	−0.051 (−0,089, −0.013)	0.0079
All (n = 48,061)	−0.035 (−0.056, −0.015)	0.0008

[1] β Coefficients and 95% CIs (cm/y) are for comparisons of effects between one category and the adjacent category for overall physical activity (eg, from inactive to moderately inactive). Data were analyzed by mixed-effects linear regression. Average physical activity energy expenditures measured by the individually calibrated combined heart rate and movement sensing in an independent validation study (n = 1941) across categories of physical activity in men and women, respectively, were as follows: inactive (38.1 and 39.2 $kJ \cdot kg^{-1} \cdot d^{-1}$), moderately inactive (47.5 and 39.9 $kJ \cdot kg^{-1} \cdot d^{-1}$), moderately active (48.5 and 44.7 $kJ \cdot kg^{-1} \cdot d^{-1}$), and active (56.8 and 49.3 $kJ \cdot kg^{-1} \cdot d^{-1}$).

baseline difference between one category of physical activity (eg, inactive compared with moderately inactive) reduced risk of becoming obese by 7% and 10% in men and women, respectively.

The major strengths of this study included its prospective design, the large and diverse sample that included participants from 9 European countries, the extensive assessment of potential confounding variables, and our consistent and valid measure of physical activity across study locations. It is unlikely that the differential results for the association between physical activity and changes in body weight and waist circumference are explained by differences in the number of individuals included in the analyses. This is because these differences were consistent when we restricted the analyses to those 5 study locations from which data on body weight and waist circumference were available (data not shown). However, self-reported body weight and waist circumference may be reported with different degrees of accuracy although self-reported body weight is highly correlated with measured weight (21). Indeed, if this was the case, the beneficial effect of increasing physical activity may not have been restricted to subjects who were of normal-weight at baseline. However, in keeping with our results, Lee et al (11) recently concluded that physical activity was associated with less weight gain in women whose BMI was <25 but not in women who were overweight or obese.

Our study was limited by its observational design and could not prove causality for the observed protective effect of physical activity on a gain in central adiposity. Indeed, higher levels of central and overall adiposity at baseline may lead to lower levels of physical activity at follow up as recently suggested for objectively measured total sedentary time (22). Furthermore, the self-reported nature of some covariates (eg, example dietary intake) may have resulted in residual confounding. Physical activity was only measured at baseline, and any change in this behavior between baseline and follow-up may have led to misclassification and, therefore, the attenuation of associations observed. Our population was a subsample of the original EPIC cohort and may not have been representative for the EPIC cohort as whole or the general population. Finally, a significant heterogeneity between study locations was observed in both men and women. Possible sources of heterogeneity included biological diversity in cohorts, differences in sample size, differences in measurements of the outcome variable, or chance. Nevertheless, our observation that physical activity was differentially associated with gains in body weight and waist circumference was supported by the similar effect sizes for both outcomes in the 2 cohorts that measured body weight and waist circumference at follow-up.

Sternfeld et al (23) reported that a one-unit increase in self-reported sport and exercise participation was associated with a nonsignificant decrease of 0.10 cm in waist circumference after 3 y in middle-aged US women. In contrast, Koh-Banerjee et al (24) reported that an increase in physical activity of 25 metabolic equivalent task hours per week (≈4 h of jogging/wk) between baseline and follow-up was associated with a 0.91-cm decrease in waist circumference over a 9-y follow-up period in US men aged 40–75 y. However, the latter study examined the associations between changes in the exposure variable (ie, physical activity) with changes in waist circumference that precluded the possibility to determine whether baseline physical activity was truly a determinant of a change in waist circumference.

Increasing physical activity over time may not necessarily reduce body weight but, rather, induce changes in body composition and body fat distribution. In keeping with this, lifestyle interventions have shown significant reductions in waist circumferences in the absence of changes in body weight or fat mass after increased physical activity (25–28). The effect on abdominal adiposity by increasing physical activity was consistent with studies that suggested that moderate intensity exercise was associated with an increase in lipolysis in subcutaneous abdominal adipose tissue compared with in femoral adipose tissue (29, 30).

The effect size of physical activity on waist gain observed in this study may be considered trivial and not clinically meaningful. The difference between being categorized as physically inactive and being categorized as moderately inactive was associated with a decrease in waist circumference of 0.15–0.20 cm over 5 y of follow-up independent of the baseline waist circumference, body weight, and other confounding factors. This

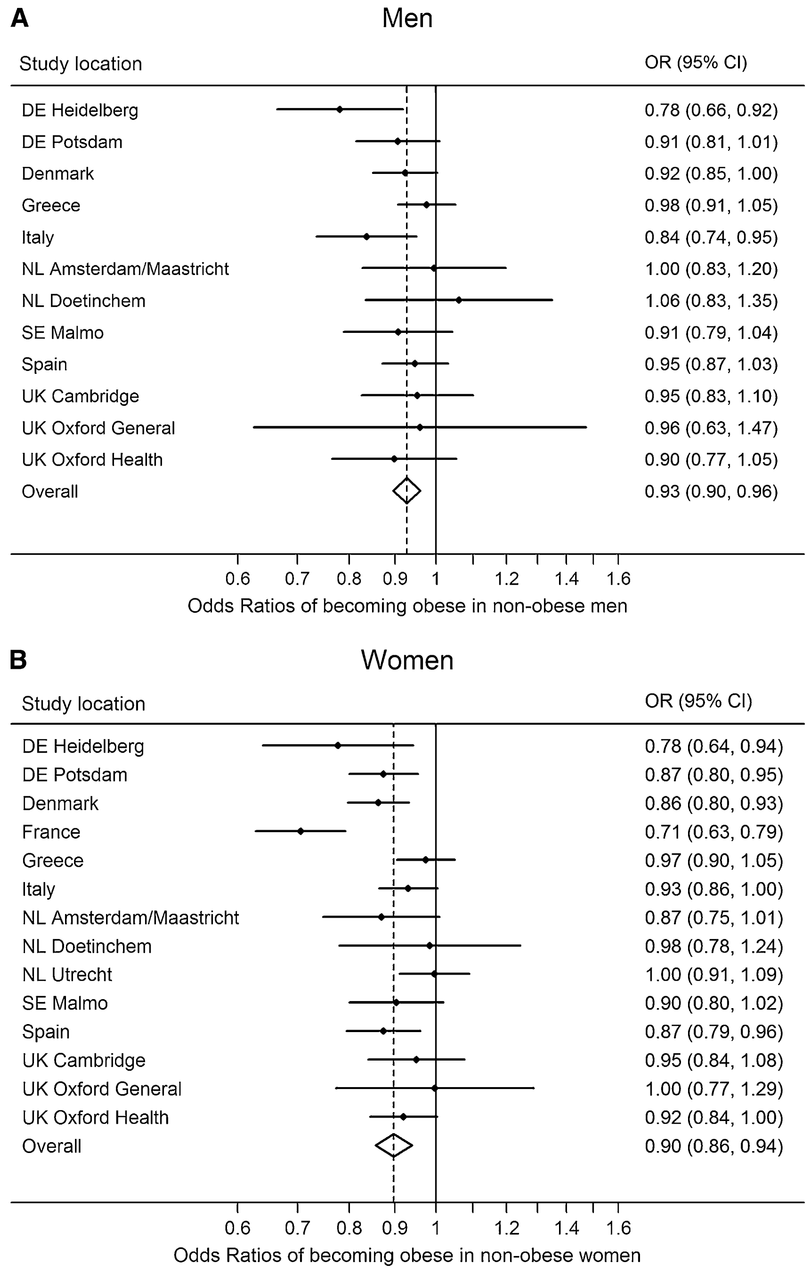

FIGURE 3. Odds ratios (OR; analyzed by logistic regression) of becoming obese in nonobese men (A) (overall $P < 0.001$, $n = 71{,}179$) and women (B) (overall $P < 0.001$, $n = 178{,}927$) per one-category increment in overall physical activity after adjustment for age, smoking, energy intake, alcohol consumption, educational level, and duration of follow-up. A significant heterogeneity by country was observed in women ($I^2 = 61.1\%$, $P = 0.0015$). Average physical activity energy expenditures measured by the individually calibrated combined heart rate and movement sensing in an independent validation study ($n = 1941$) across categories of physical activity in men and women, respectively, were as follows: inactive (38.1 and 39.2 $kJ \cdot kg^{-1} \cdot d^{-1}$), moderately inactive (47.5 and 39.9 $kJ \cdot kg^{-1} \cdot d^{-1}$), moderately active (48.5 and 44.7 $kJ \cdot kg^{-1} \cdot d^{-1}$), and active (56.8 and 49.3 $kJ \cdot kg^{-1} \cdot d^{-1}$). DE, Germany; NL, Netherlands; SE, Sweden.

equated to ≈3–5% of the total gain in waist circumference between baseline and follow-up. However, these effect estimates were likely to be underestimated because of random measurement errors in the exposure variable. Physical activity was only measured once in this study, and even if our preliminary validation results suggested that our 4-category index was valid for ranking individuals, this index explained <10% of the total variance in PAEE. Furthermore, our calibration results suggested that the difference between moving from one category to the next of self-reported physical activity was equal to an increase of PAEE of ≈75 kcal/d for an individual with a body weight of 70 kg (PH Peeters, NJ Wareham, and U Ekelund, personal communication, 2 November 2010), which equated to ≈15 min of brisk walking.

Our results may have implications for public health. The effect of physical activity on the gain in waist circumference was linear across physical activity categories and observed in men and women, across age groups and in normal-weight, overweight, and obese groups. This suggested that even relatively small changes in physical activity may have beneficial effects on central adiposity. Combined with observations that abdominal adiposity conveys the greatest health risks (6–8), our results suggested that increasing physical activity independent of a change in body weight may be a useful strategy for preventing premature mortality and metabolic and other chronic diseases.

In conclusion, higher levels of physical activity consistently predicted a lower gain in waist circumference in normal-weight, overweight, and obese individuals independent of the baseline and concomitant change in body weight. The effect of physical activity on a gain in body weight may be restricted to younger and normal-weight individuals. Overall, physical activity is a useful strategy for preventing metabolic and other chronic diseases and premature death through its effect on central adiposity.

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REFERENCES

1. International Obesity Task Force. Adult overweight and obesity in the European Union (EU27). Available from: http://www.iotf.org/database/documents/AdultEU27May09pdf.pdf (cited 20 April 2010).
2. Berghöfer A, Pischon T, Reinhold T, Apovian CM, Sharma AM, Willich SN. Obesity prevalence from a European perspective: a systematic review. BMC Public Health 2008;8:200.
3. Frayling TM, Timpson NJ, Weedon MN, et al. A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. Science 2007;316:889–94.
4. Willer CJ, Speliotes EK, Loos RJ, et al. Six new loci associated with body mass index highlight a neuronal influence on body weight regulation. Nat Genet 2009;41:25–34.
5. Loos RJ, Lindgren CM, Li S, et al. Common variants near MC4R are associated with fat mass, weight and risk of obesity. Nat Genet 2008;40:768–75.
6. Wang Y, Rimm EB, Stampfer MJ, Willett WC, Hu FB. Comparison of abdominal adiposity and overall obesity in predicting risk of type 2 diabetes among men. Am J Clin Nutr 2005;81:555–63.
7. Yusuf S, Hawken S, Ounpuu S, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2005;366:1640–9.
8. Pischon T, Boeing H, Hoffmann K, et al. General and abdominal adiposity and risk of death in Europe. N Engl J Med 2008;359:2105–20.
9. Wareham NJ, van Sluijs E, Ekelund U. Physical activity and obesity prevention: a review of the current evidence. Proc Nutr Soc 2005;64:229–47.
10. Summerbell CD, Douthwaite W, Whittaker V, et al. The association between diet and physical activity and subsequent excess weight gain and obesity assessed at 5 years of age or older: a systematic review of the epidemiological evidence. Int J Obes (Lond) 2009;33(suppl 3):S1–92.
11. Lee IM, Djoussé L, Sesso HD, Wang L, Buring JE. Physical activity and weight gain prevention. JAMA 2010;303:1173–9.
12. Ferrari P, Slimani N, Ciampi A, et al. Evaluation of under- and over-reporting of energy intake in the 24-hour diet recalls in the European Prospective Investigation into Cancer and Nutrition (EPIC). Public Health Nutr 2002;5(6B):1329–45.
13. Besson H, Ekelund U, Luan JA, et al. A cross-sectional analysis of physical activity and obesity indicators in European participants of the EPIC-PANACEA study. Int J Obes 2009;33:497–506.
14. Haftenberger M, Lahmann PH, Panico S, et al. Overweight, obesity and fat distribution in 50- to 64-year-old participants in the European Prospective Investigation into Cancer and Nutrition (EPIC). Public Health Nutr 2002;5(6B):1147–62.
15. Haftenberger M, Schuit AJ, Tormo MJ, et al. Physical activity of subjects aged 50-64 years involved in the European Prospective Investigation into Cancer and Nutrition (EPIC). Public Health Nutr 2002;5(6B):1163–76.
16. Wareham NJ, Jakes RW, Rennie KL, et al. Validity and repeatability of a simple index derived from the short physical activity questionnaire used in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Public Health Nutr 2003;6:407–13.
17. Brage S, Brage N, Franks PW, et al. Branched equation modelling of simultaneous accelerometry and heart rate monitoring improves estimate of directly measured physical activity energy expenditure. J Appl Physiol 2004;96:343–51.
18. Brage S, Ekelund U, Brage N, et al. Hierarchy of individual calibration levels for heart rare and accelerometry to measure physical activity. J Appl Physiol 2007;103:682–92.
19. Khaw KT, Jakes R, Bingham S, et al. Work and leisure time physical activity assessed using a simple, pragmatic, validated questionnaire and incident cardiovascular disease and all-cause mortality in men and women: The European Prospective Investigation into Cancer in Norfolk prospective population study. Int J Epidemiol 2006;35:1034–43.
20. Slimani N, Deharveng G, Unwin I, et al. The EPIC nutrient database project (ENDB): a first attempt to standardize nutrient databases across the 10 European countries participating in the EPIC study. Eur J Clin Nutr 2007;61:1037–56.
21. Spencer EA, Appleby PN, Davey GK, Key TJ. Validity of self-reported height and weight in 4808 EPIC-Oxford participants. Public Health Nutr 2002;5:561–5.
22. Ekelund U, Brage S, Besson H, Sharp S, Wareham NJ. Sedentary time and weight gain in healthy adults; reverse or bidirectional causality? Am J Clin Nutr 2008;88:612–7.
23. Sternfeld B, Wang H, Quesenberry CP Jr, et al. Physical activity and changes in weight and waist circumference in midlife women: findings from the Study of Women's Health Across the Nation. Am J Epidemiol 2004;160:912–22.
24. Koh-Banerjee P, Chu NF, Spiegelman D, et al. Prospective study of the association of changes in dietary intake, physical activity, alcohol consumption, and smoking with 9-y gain in waist circumference among 16 587 US men. Am J Clin Nutr 2003;78:719–27.
25. Ross R, Janssen I, Dawson J, et al. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. Obes Res 2004;12:789–98.
26. Church TS, Earnest CP, Skinner JS, Blair SN. Effects of different doses of physical activity on cardio-respiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. JAMA 2007;297:2081–91.
27. Eriksson MK, Franks PW, Eliasson M. A 3-year randomized trial of lifestyle intervention for cardiovascular risk reduction in the primary care setting: the Swedish Björknäs study. PLoS ONE 2009;4:e5195.
28. Ross R, Bradshaw AJ. The future of obesity reduction: beyond weight loss. Nat Rev Endocrinol. 2009;5:319–25.
29. Arner P, Kriegholm E, Engfeldt P, Bolinder J. Adrenergic regulation of lipolysis in situ at rest and during exercise. J Clin Invest 1990;85:893–8.
30. Horowitz JF, Leone TC, Feng W, Kelly DP, Klein S. Effect of endurance training on lipid metabolism in women: a potential role for PPARalpha in the metabolic response to training. Am J Physiol Endocrinol Metab 2000;279:E348–55.