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ORIGINAL ARTICLE

A cross-sectional analysis of physical activity and obesity indicators in European participants of the EPIC-PANACEA study

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Objectives: Cross-sectional data suggest a strong association between low levels of physical activity and obesity. The EPIC-PANACEA (European Prospective Investigation into Cancer-Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating out of home And obesity) project was designed to investigate the associations between physical activity and body mass index (BMI) and waist circumference based on individual data collected across nine European countries.

Methods: In the European Prospective Investigation into Cancer and Nutrition (EPIC), 519 931 volunteers were recruited between 1992 and 2000, of whom 405 819 had data on main variables of interest. Height, body weight and waist circumference were measured using standardized procedures. Physical activity was assessed using a validated four-category

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index reflecting a self-reported usual activity during work and leisure time. The associations between physical activity and BMI and waist circumference were estimated using multilevel mixed effects linear regression models, adjusted for age, total energy intake, smoking status, alcohol consumption and educational level.
Results: A total of 125 629 men and 280 190 women with a mean age of 52.9 (s.d. 9.7) and 51.5 (s.d. 10.0) years, respectively were included. The mean BMI was 26.6 kg/m^2 (s.d. 3.6) in men and 25.0 kg/m^2 (s.d. 4.5) in women. Fifty percent of men and 30% of women were categorized as being active or moderately active. A one-category difference in the physical activity index was inversely associated with a difference of 0.18 kg/m^2 in the mean BMI (95% confidence interval, CI, 0.11, 0.24) and 1.04-cm (95% CI 0.82, 1.26) difference in waist circumference in men. The equivalent figures for women were 0.31 kg/m^2 (95% CI 0.23, 0.38) and 0.90 cm (95% CI 0.71, 1.08), respectively.
Conclusions: Physical activity is inversely associated with both BMI and waist circumference across nine European countries. Although we cannot interpret the association causally, our results were observed in a large and diverse cohort independently from many potential confounders.
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Keywords: physical activity; BMI; waist circumference; cross-sectional analysis; Europe

Introduction

In 2005, the World Health Organization estimated that the number of obese individuals (body mass index, BMI, $\geqslant$30 kg/m^2) aged above 15 years was at least 400 million, with projections for 2015 increasing this figure to more than 700 million worldwide.[1] Recently, a surveillance study based on data in 22 777 continental Europeans over the age of 50 years reported prevalence figures of obesity ranging from 12.8% in Sweden to 20.2% in Spain for men and from 12.3% in Switzerland to 25.6% in Spain for women.[2] As overweight (BMI, 25.0–29.9 kg/m^2) and obesity (BMI, $\geqslant$30 kg/m^2) are associated with cardiovascular diseases, type 2 diabetes, osteoarthritis and some cancers,[3] their prevention is a major public health priority.

The two main established risk factors for overweight and obesity are excess of energy intake from foods and drinks and low energy expenditure because of the lack of physical activity.[4] Earlier studies examining the cross-sectional associations between body fat indices and physical activity have suggested an inverse dose-response association.[4] However, prevalence studies of self-reported physical activity[5] and of obesity[2,6] across European countries do not report systematically the lowest prevalence of obesity, in countries characterized by the highest level of physical activity and vice versa. In addition, both physical activity and obesity are age and sex dependent.[7–9] It is, therefore, reasonable to hypothesize that the association between physical activity and obesity varies between age and sex groups as observed in earlier studies.[10,11]

Therefore, the aim of this study was to examine the associations between self-reported physical activity and measured BMI and waist circumference, the most commonly used estimates of overall and abdominal fatness, using cross-sectional data collected from more than 400 000 men and women from nine European countries, as part of the EPIC-PANACEA (European Prospective Investigation into Cancer-Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating out of home And obesity) study. The EPIC study was designed to examine relationships between nutrition, hormones, genotype and the occurrence of chronic diseases. The EPIC sample is heterogeneous in respect to several socio-demographical and anthropometric variables and provides detailed information on several lifestyle factors. This provides a unique opportunity to examine the relationship between several lifestyle factors and obesity. Here, we report on the cross-sectional associations between physical activity with obesity, and whether this association is similar across different European countries. The results from this study have the potential to increase our knowledge on how the association between physical activity and obesity may differ by sex, age, geographical and cultural contexts independently of several potential confounders.

Material and methods

The EPIC study is an ongoing multicentre prospective cohort study conducted in 23 centres in 10 European countries (Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, Spain, Sweden and United Kingdom). Between 1992 and 2000, with minor differences in time between countries and centres, 519 931 eligible male and female participants were recruited. Exceptions were the French cohort (based on female members of a health insurance for school employees), the Utrecht cohort from The Netherlands (based on women attending breast cancer screening), the Greek cohort (including individuals recruited from all regions of the country) and part of the Oxford cohort in the United Kingdom (based on vegetarian volunteers and healthy eaters). In addition, several Spanish and Italian centres were partly based on blood donors, and the Italian cohort from Florence also included breast cancer screening participants. In France, Norway, Utrecht (The Netherlands) and Naples (Italy), only women were recruited. A description of the data collection methods used in the EPIC study has been reported earlier.[12] All participants provided their written informed consent. Approval for this study was obtained from the ethical review

Table 1 Interpretation of the physical activity index

Work activity	*Leisure time physical activity (duration of sport and cycling in hours/day)*			
	No	*⩽0.5*	*>0.5 and ⩽1.0*	*>1.0*
No or sedentary job	Inactive	Moderately inactive	Moderately active	Active
Standing job	Moderately inactive	Moderately active	Active	Active
Manual job	Moderately active	Active	Active	Active
Heavy manual job	Active	Active	Active	Active

boards of the International Agency for Research on Cancer and from all local institutions, in which participants had been recruited for the EPIC study.

Study population
Following the PANACEA project exclusion criteria, from the 519 931 participants recruited initially, we excluded participants without data on dietary intake ($n=6611$), with extreme ratio of energy intake to estimated energy requirement (observations in the top and bottom 0.5%)[13] ($n=10\,209$), without information on smoking status, alcohol consumption and educational level available ($n=64$) and pregnant women ($n=623$). Information on self-reported physical activity was not used for all participants from Norway ($n=36\,449$) and Umea in Sweden ($n=25\,216$), their questionnaires being too different from the common standardized EPIC questionnaire. We also excluded 340 individuals with extreme data on anthropometric variables (that is, weight >250 kg and/or height <130 cm, BMI <16 kg/m^2 and/or waist circumference <40 cm and/or waist circumference >160 cm and/or waist circumference <60 cm associated with BMI >25 kg/m^2). Finally, we excluded all participants without available information on physical activity ($n=7125$), BMI ($n=3864$) and selected confounding variables ($n=23\,611$). Here, of the remaining 405 819 individuals, no measure of waist circumference was available in 68 411 participants. Thus, in this paper, the analyses investigating the association between physical activity and BMI were based on 405 819 individuals, and those examining the association between physical activity and waist circumference were restricted to 337 408 participants. Nine countries participated in the EPIC-PANACEA project: in Greece, Sweden and also in The Netherlands for analyses restricted to men, there was only one centre that recruited participants into this study, whereas in the other countries two or more regions recruited participants.

Physical activity assessment
The assessment of physical activity in the EPIC has been described earlier in detail.[14,15] Briefly, physical activity data were obtained from either in-person interviews or self-administered using a standardized questionnaire. In the centres in Malmö (Sweden) and Naples (Italy), the format of the physical activity questions was somewhat different compared with that in the other centres (categorical frequencies and durations rather than continuous). However, these data were transformed and combined with the data from the remaining centres, before analyses.

Total physical activity was assessed using three questions referring to activity during the past year. The first question asked about usual physical activity at work, classified as four categories: sedentary, standing (for example, hairdresser, shop assistant, guard), physical work (for example, plumber, cleaner, nurse) and heavy manual work (for example, docker, construction worker, bricklayer). The two other questions asked about the amount of time in hours per week during winter and summer spent in (1) cycling, and (2) other physical exercises (for example, keep fit, jogging, swimming). The average time spent daily in recreational activity per day was estimated as the mean of the self-reported total hours per week during winter and summer, divided by seven. A physical activity index was derived by allocating individuals into four ordered categories of overall activity as described in Table 1. All other variables from the questionnaire that is, walking, gardening, do it yourself, housework and climbing stairs were not correlated significantly with objective measurement of physical activity, and were consequently not used to compute the physical activity index.[15] This index was positively and significantly correlated with objective measures of the ratio of daytime energy expenditure to resting metabolic rate (dayPAR) ($P=0.003$).[15]

Anthropometry assessment
Body weight and height were measured according to standardized procedures as earlier described.[16] Briefly, weight was measured to the nearest 0.1 kg and height was measured to the nearest 0.1, 0.5, or 1.0 cm depending on the study centre, without shoes. Waist circumference was 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 the centres because of different procedures, when measuring height and weight as earlier described.[16] Briefly, for subjects who were dressed normally and were without shoes, 1.5 kg for weight and 2.0 cm for circumferences were subtracted from the original measurement, whereas for subjects in light clothing without shoes,

1 kg was subtracted from the weight. For a part of the Oxford (United Kingdom) cohort, linear regression models were used to predict sex- and age-specific values in subjects with both measured and self-reported body measures.[16–18] Of the 405 819 individuals included in this report, self-reported body measures, instead of measured height and weight, was used in a subsample of 66 199 (16.3%) and in 731 (0.2%) participants for waist circumference. The BMI was calculated as weight in kilograms divided by metres squared (kg/m^2).

Assessment of confounders

Lifestyle and socio-demographic characteristics, including education, medical history, smoking status (current, ex, or never smoker) were assessed at the study entry for all participants in the cohort. Diet and alcohol consumption over the previous 12 months were assessed at the time of enrolment, using dietary food frequency questionnaires specifically developed and validated in each participating country.[12]

Statistical methods

Baseline characteristics of the study sample were summarized separately for men and women using means and s.d. for continuous variables, and frequencies and percentages for categorical variables.

The association between physical activity (determinant) and BMI (outcome, continuous) across all countries combined was estimated using a multilevel mixed effects linear regression model. Methods of weight, height and waist circumferences, as well as physical activity questions differed slightly between centres and countries; therefore, 'centres in a country' were included as the second level and 'countries' as the third level ('individuals' are the first level) in the analyses. Physical activity was treated as an ordered variable in all models, as when it was included as a categorical variable with four levels (three indicator variables), the difference in effect between each category was similar.

The association between physical activity and BMI was thereafter estimated separately in each country using a generalized linear regression model, if the country had one centre (or region). If the country had more than one centre (or region), the interaction between physical activity and centre (region) was tested; if it was statistically significant ($P<0.05$), a mixed effects linear regression model with random slopes was introduced which allows (1) the centre effects (intercepts) to be random; and (2) the effects of physical activity (slopes) to be random and to differ between centres; if the interaction was not significant, mixed effects linear regression model with random intercept was applied that allows the centre effects to be random, whereas assuming a common effect of physical activity for all centres. The extent of heterogeneity between country-specific estimates of the association was tested.

All models included the following potential confounders (as fixed effects): smoking status (never smoker, ex-smoker, current smoker), alcohol consumption at recruitment in a six-level variable for women (0 g day^{-1}; up to 6 g day^{-1}; 7–18 g day^{-1}; 19–30 g day^{-1}; 31–60 g day^{-1}; over 60 g day^{-1}) and a seventh-level variable for men (0 g day^{-1}; up to 6 g day^{-1}; 7–18 g day^{-1}; 19–30 g day^{-1}; 31–60 g day^{-1}; 61–96 g day^{-1}; over 96 g day^{-1}), highest educational level achieved (none; primary school; technical professional school; other secondary school; and higher education), age at recruitment (years) and total energy intake (kcal day^{-1}).

The analyses were carried out separately for (1) men; (2) women; (3) men aged <60 years; (4) men aged $\geqslant 60$ years; (5) women aged <60 years; and (6) women aged $\geqslant 60$ years. The estimated association within each country, together with a combined estimate and confidence intervals (CIs), were displayed using forest plots. A similar analysis was then carried out to estimate the association between physical activity and waist circumference.

A sensitivity analysis was carried out excluding participants reporting at the study entry with a history of diabetes, cancer, heart disease or stroke, and another analysis excluded those with self-reported anthropometric measures.

Results

Characteristics of study participants

Table 2 displays the number of participants stratified by gender, age group and country. The analysis of the association between physical activity and BMI was based on 280 190 women and 125 629 men. The analysis of the association between physical activity and waist circumference was based on 212 997 women and 124 411 men. With the exception of the analyses based on Dutch men over 60 years old and French analyses focussed on waist circumference, within each country, for each gender and all age groups for both BMI and waist circumference, analyses were based on at least 1500 participants.

Overall, 22.5% of the participants were obese, (that is, BMI, $\geqslant 30$ kg/m^2, or waist circumference $\geqslant 88$ cm for women, or waist circumference $\geqslant 102$ cm for men). The lowest prevalence values were observed in France (3.6%) and in the United Kingdom (12.6%). In contrast, 44.5 and 47.1% of the Spanish and the Greek participants, respectively, were categorized as obese. It should be noted that the EPIC is not a representative sample of the general population in each country. Regardless of country, the prevalence values of obesity by increasing category of physical activity were 33.4, 20.7, 17.7 and 18.8%, respectively. Table 3 shows the characteristics of the study participants by the level of physical activity for men and women separately. For both men and women, active participants were 3 years younger than the inactive ones. When comparing the active with the inactive men, differences in means were -0.4 kg/m^2 for BMI and -2.2 cm for waist circumference. Among women, these differences were, respectively, three times and 50% greater than those observed for men. For both men and women,

Table 2 Number of participants with complete information by gender, age group and country in the EPIC-PANACEA study

	Number of participants measured for both BMI and physical activity[a]			*Number of participants measured for both waist circumference and physical activity*[a]		
	<60 years old	*⩾60 years old*	*All ages combined*	*<60 years old*	*⩾60 years old*	*All ages combined*
Men						
France (0 centre)	0	0	0	0	0	0
Italy (four centres)	12 300	1688	13 988	11 403	1625	13 028
Spain (five centres)	12 716	1971	14 687	12 697	1970	14 667
United Kingdom (two centres)	13 490	6363	19 853	13 319	6338	19 657
The Netherlands (one centre)	7494	229	7723	7484	229	7713
Greece (one centre)	6504	3484	9988	6501	3483	9984
Germany (two centres)	17 482	4717	22 199	17 471	4713	22 184
Sweden (one centre)	5757	5000	10 757	5754	4996	10 750
Denmark (two centres)	19 518	6916	26 434	19 515	6913	26 428
All	95 261	30 368	125 629	94 144	30 267	124 411
Women						
France (six centres)	53 762	11 724	65 486	391	107	498
Italy (five centres)	26 918	4301	31 219	26 638	4277	30 915
Spain (five centres)	21 328	2446	23 774	21 305	2443	23 748
United Kingdom (two centres)	36 263	8022	44 285	34 527	7951	42 478
The Netherlands (two centres)	19 635	6283	25 918	19 618	6279	25 897
Greece (one centre)	9155	5343	14 498	9151	5337	14 488
Germany (two centres)	24 597	4773	29 370	24 576	4772	29 348
Sweden (one centre)	10 092	6488	16 580	10 087	6484	16 571
Denmark (two centres)	21 113	7947	29 060	21 111	7943	29 054
All	222 863	57 327	280 190	167 404	45 593	212 997

Abbreviations: European Prospective Investigation into Cancer-Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating out of home And obesity; BMI, body mass index. [a]In addition to measurement for smoking status, alcohol consumption, educational level, age and total energy intake.

energy intake tended to be slightly greater among the active participants. Active women were more educated, had a lower percentage of never smokers and consumed more alcohol than inactive women. Compared with inactive men, active men were less educated, consumed slightly more alcohol but had similar patterns of tobacco consumption.

Estimates of the association

Physical activity was inversely associated with the BMI in men and women (Figure 1). For a one-category difference in the physical activity index, the mean BMI was 0.31 kg/m^2 (95% CI 0.23–0.38) lower in women and 0.18 kg/m^2 (95% CI 0.11–0.24) lower in men. There was a significant inverse association across all countries except in the Greek men. Significant heterogeneity between countries was observed in women but not in men. The magnitude of the association between physical activity and BMI was similar in younger and older men (data not shown). In younger men (<60 years), the association between physical activity and BMI was significant in each country. In older men, the association with BMI was significant in each country except in The Netherlands and in Greece.

In women, the magnitude of the association was similar between the two age groups (data not shown). Heterogeneity between countries was greater in younger women ($P = 2.7 \times 10e^{-12}$) compared with that in older women ($P = 0.01$). The association between physical activity and BMI was significant in all countries, except for the older Spanish women ($P = 0.09$).

The physical activity index was significantly inversely associated with waist circumference (Figure 2). For a one-level difference in the physical activity index, waist circumference was lowered by 0.90 cm (95% CI 0.71–1.08) in women and by 1.04 cm (95% CI 0.82–1.26) in men. This association was significant in all countries, and no heterogeneity between countries was observed in either men or women.

The magnitude of the association was similar between age groups in men (data not shown). This association was statistically significant in younger and older men in all countries except in the 229 older men in The Netherlands. In older men, significant heterogeneity between countries was observed ($P = 0.007$).

In women (data not shown), the magnitude of the association was slightly weaker in younger women (−0.88; 95% CI −1.06 to −0.69) compared with that in older women (−1.09; 95% CI −1.20 to −0.98). Significant heterogeneity between countries was observed in the older but not in the younger age group. The association between physical activity and waist circumference was inversely and statistically significant in all countries and age groups except for younger women in The Netherlands and older French women.

Post hoc *analyses*

The inverse relationship between physical activity and obesity indicators was attenuated only when occupational activity was included in the index. Moving from one intensity level of

Table 3 Characteristics of men and women in the EPIC-PANACEA study

	Men				Women			
	Inactive or moderately inactive (n = 63 015)		*Active or moderately active (n = 62 614)*		*Inactive or moderately inactive (n = 168 324)*		*Active or moderately active (n = 111 866)*	
	Mean	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*
Age (years)	54.6	9.8	51.3	9.3	52.6	10.0	49.8	9.6
BMI (kg/m^2)	26.8	3.7	26.4	3.5	25.5	4.7	24.3	4.0
Waist circumference (cm)	95.9	10.3	93.7	9.9	81.9	11.9	78.6	10.7
Energy intake (kcal day^{-1})	2362.1	638.4	2529.1	674.4	1975.2	542.0	2010.0	537.8
	N	%	n	%	n	%	n	%
School level								
None	3006	4.8	2309	3.7	11 954	7.1	1654	1.5
Primary school	16 513	26.2	18 541	29.6	42 905	25.5	20 836	18.6
Technical/professional school	14 233	22.6	17 223	27.5	31 717	18.8	27 589	24.7
Other secondary school	9907	15.7	8920	14.3	44 357	26.4	29 624	26.5
Higher education	19 356	30.7	15 621	25.0	37 391	22.2	32 163	28.8
Smoking status								
Never smoker	18881	30.0	20 036	32.0	103 046	61.2	62 230	55.6
Ex-smoker	24541	38.9	23 378	37.3	34 210	20.3	28 563	25.5
Current smoker	19593	31.1	19 200	30.7	31 068	18.5	21 073	18.8
Alcohol consumption								
0 g day^{-1}	4956	7.9	3457	5.5	33 593	20.0	12 104	10.8
0< g day^{-1} <6	13 537	21.5	11 948	19.1	66 117	39.3	45 094	40.3
6< g day^{-1} <18	17 905	28.4	17 812	28.5	43 515	25.9	35 278	31.5
18< g day^{-1} <30	10 045	15.9	10 732	17.1	14 265	8.5	10 614	9.5
30< g day^{-1} <60	11 796	18.7	12 933	20.7	9541	5.7	7806	7.0
60< g /day^{-1} <96	3589	5.7	4267	6.8	1293	0.8	970	0.9
96< g day^{-1}	1187	1.9	1465	2.3				

Abbreviations: European Prospective Investigation into Cancer-Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating out of home And obesity; BMI, body mass index.

physical activity at work to the next, corresponded to a difference in the BMI of $+0.04\,kg/m^2$ ($P=0.001$) among men and of $+0.01\,kg/m^2$ ($P=0.22$) among women. Similar results were observed with waist circumference. A total of 36 360 subjects had a history of heart disease, stroke, diabetes or cancer. Exclusion of these individuals did not significantly alter the associations. Corresponding β coefficients (95% CI) for a one-level difference in the physical activity index were −0.29 (−0.37; −0.21) and −0.85 (−1.04; −0.66) among women and −0.17 (−0.23; −0.11) and −1.02 (−1.23; −0.82) among men for BMI and waist circumference, respectively. We re-analyzed our data after excluding participants for whom, only self-reported data on height and weight were available and the results remained unchanged.

Discussion

In the cross-sectional analyses of data from nine European countries comprising more than 400 000 men and women, we observed a strong inverse association between total physical activity and BMI and waist circumference. These inverse associations were independent of age, smoking status, alcohol consumption, educational level, energy intake and study centre, and were observed within each country for both men and women separately. Although slightly different between gender and age groups, moving from one level of physical activity to the next corresponded to a difference of 1 cm in waist circumference and to a difference of $0.25\,kg/m^2$ in the BMI.

Our study has several methodological strengths. First, it is unlikely that the associations observed here are because of chance, owing to the large sample size comprising 405 819 individuals from nine different countries. Second, our results are similar in magnitude between men and women and consistent across countries and age groups. Third, excluding participants with self-reported data on height and weight and those reporting any history of diabetes, cancer, heart disease or stroke did not materially change our results. Fourth, we adjusted our analyses for a number of putative confounders including alcohol consumption, smoking and energy intake. Finally, examining these associations in a European population-based cohort makes the results more generalizable compared with that in single country studies.

Consideration must be given to the potential limitations of this study, including its cross-sectional approach. We cannot establish a causal association between physical

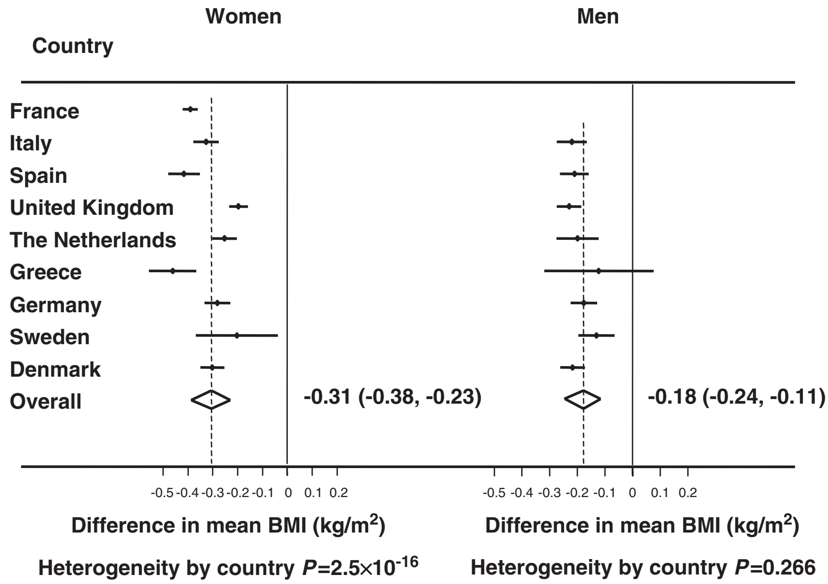

Figure 1 Association between a one-category difference of the four-level physical activity index and body mass index (BMI, kg/m^2) by gender and all ages combined in the EPIC-PANACEA (European Prospective Investigation into Cancer-Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating out of Home and Obesity) study; after adjustment for smoking status, alcohol consumption, educational level, age and total energy intake.

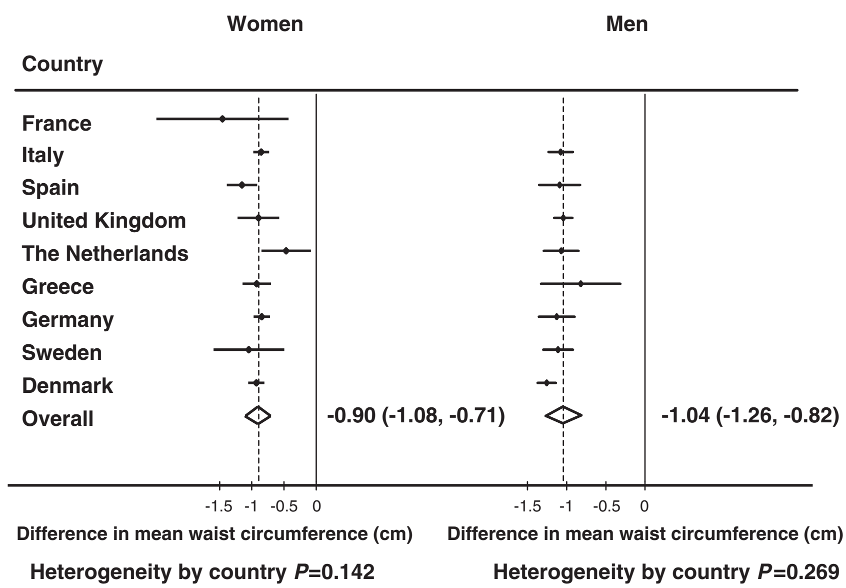

Figure 2 Association between a one-category difference of the four-level physical activity index and waist circumference (cm) by gender and all ages combined in the EPIC-PANACEA (European Prospective Investigation into Cancer-Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating out of Home and Obesity) study; after adjustment for smoking status, alcohol consumption, educational level, age and total energy intake.

activity and obesity or the direction of association. Although we adjusted our analyses for confounders, we cannot rule out the possibility that other unmeasured confounders such as genotype, birth weight and early growth explain the observed associations. An important aspect of this study is that physical activity was self-reported. Although the questionnaire has been shown to be valid for ranking participants, the level of measurement error was considerable.[15] We cannot exclude the possibility of differential measurement error because of obesity. However, if overweight and obese individuals over-report their activity levels, this will only attenuate the observed inverse associations. In general, physical activity questionnaires with similar measurement characteristics of the EPIC questionnaire have been shown to lead to attenuation of the associations between physical activity and the outcome of interest.[19] Therefore, it is unlikely that the observed inverse relationship between physical activity and obesity is explained by reporting bias. Finally, the validity of the physical activity questionnaire has not been tested rigorously in all study locations.[15] However, the consistent associations between physical activity and obesity indicators in the expected direction across countries suggest the questionnaire has face validity.

Our findings of an inverse relationship between physical activity and BMI are consistent with the literature. In population-based studies, individuals who report higher levels of leisure time physical activity or regular participation in exercise tend to be leaner,[20,21] although the magnitude of association appears to be small.[22] The inverse relationship observed between the physical activity index and obesity indicators appeared to be influenced by cycling and other exercises to a larger extend than by occupational activity. This is consistent with another recent European study reporting an inverse association between leisure time physical activity and obesity, but not with physical activity at work.[23] This may be explained by a true stronger influence of leisure time physical activity on obesity, misclassification by occupational status or a combination of both. However, domain-specific results based on single items should be interpreted cautiously.

Our study is unique, as it is the first to examine this relationship at a European level using individual data. With few exceptions, including Greek and Dutch men and Spanish women older than 60 years of age, the inverse relationship was consistent within each country amongst men and women and in younger and older participants.

The lack of significant associations in some subgroups is likely to be explained by statistical artefacts. Most likely, we did not have the power to detect an association in the older Dutch men ($n=229$), and the insertion of the interaction term for study centre in the model widened the CI in the Spanish sample.

Our observations of an inverse relationship between physical activity and waist circumference are also consistent with the literature, as numerous cross-sectional analyses reported similar results.[24–26] However, this is the first study based on individual data hitherto reporting the inverse relationship between physical activity and waist circumference at a European level. Furthermore, our results were robust to confounding, consistent across countries and remained significant after stratification by both age and gender. Strata in which results were not significant were characterized by either their small sample size or by heterogeneity by study centre, such as in younger Dutch women, in which an interaction term on centre was inserted within the model making the CI wider.

Results stratified by gender and age were comparable in direction but slightly different in magnitude. We found that the inverse relationship with waist circumference was slightly greater among men than women. There is no evidence of such a sex difference in the literature.[27] However, we could speculate that due to a more central distribution of fat among men than women,[28] a potential loss of fat due to increased physical activity would be mainly abdominal for men than for women, which is better assessed with waist circumference than with BMI. In contrast, if BMI is a better proxy for overall body fatness than for abdominal fatness, it is not surprising that the inverse association with BMI was slightly stronger in women than in men. A sex difference for the association between physical activity and BMI has earlier been reported,[29–31] although not entirely consistent.[10,32]

It is not elucidated clearly whether obesity is a cause or a consequence of physical inactivity. The imbalance between energy intake and expenditure is the main underlying cause of weight gain, and low levels of physical activity may not necessarily lead to weight gain. Prospective studies using objective measures of physical activity have not provided compelling evidence that physical inactivity is a cause of obesity.[4] In addition, it was also suggested recently that the obesity epidemic is explained likely by excess energy intake.[33] An explanation of the inverse relationship between physical activity and obesity may be that obesity incapacitates individuals from undertaking physical activity. This hypothesis is supported by results from a recent study reporting that objectively measured free-living walking distance was significantly reduced in both lean and obese individuals after experimentally induced weight gain.[34] Moreover, some prospective studies have suggested that obesity indicators predict a sedentary lifestyle.[35–37]

In summary, this study is the first characterization in a European study, suggesting physical activity is inversely related to both BMI and waist circumference independent of many confounders including energy intake. Regardless of the age, the gender and the country, for each of the four possible levels of physical activity, moving from one level to the next corresponds to a difference of 1 cm in waist circumference and a difference of $0.25\,kg/m^2$ in BMI. In concrete terms, it corresponds to about 30 extra minutes per day of cycling or a similar intense exercise. A decrease in BMI by $0.25\,kg/m^2$ for the whole study population would shift the prevalence of overweight and obesity from 49.2 to 46.8%.

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