Physical Activity and Breast Cancer Risk: The European Prospective Investigation into Cancer and Nutrition

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Abstract

There is convincing evidence for a decreased risk of breast cancer with increased physical activity. Uncertainties remain, however, about the role of different types of physical activity on breast cancer risk and the potential effect modification for these associations. We used data from 218,169 premenopausal and postmenopausal women from nine European countries, ages 20 to 80 years at study entry into the European Prospective Investigation into Cancer and Nutrition. Hazard ratios (HR) from multivariate Cox regression models were calculated using metabolic equivalent value–based physical activity variables categorized in quartiles, adjusted for age, study center, education, body mass index, smoking, alcohol use, age at menarche, age at first pregnancy, parity, current oral contraceptive use, and hormone replacement therapy use. The physical activity assessment included recreational, household, and occupational activities. A total physical activity index was estimated based on cross-tabulation of these separate types of activity. During 6.4 years of follow-up, 3,423 incident invasive breast cancers were identified. Overall, increasing total physical activity was associated with a reduction in breast cancer risk among postmenopausal women (P_{trend} = 0.06). Specifically, household activity was associated with a significantly reduced risk in postmenopausal (HR, 0.81; 95% confidence interval, 0.70-0.93, highest versus the lowest quartile; P_{trend} = 0.001) and premenopausal (HR, 0.71; 95% confidence interval, 0.55-0.90, highest versus lowest quartile; P_{trend} = 0.003) women. Occupational activity and recreational activity were not significantly related to breast cancer risk in both premenopausal and postmenopausal women. This study provides additional evidence for a protective effect of physical activity on breast cancer risk. (Cancer Epidemiol Biomarkers Prev 2007;16(1):36–42)

Introduction

The majority of epidemiologic studies indicate a reduced risk of breast cancer in relation to increased physical activity in postmenopausal women, but the evidence is less consistent in premenopausal women (1-6). Overall, the evidence of an inverse association between breast cancer risk and physical activity was in 2002 classified as ''convincing'' (7). The

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decrease in breast cancer risk for the most physically active women compared with the least active women is, on average, 20% to 40%, with some studies observing up to 70% risk reductions (7). It is hypothesized that physical activity affects breast cancer through changes in menstrual characteristics, body size, metabolism of endogenous hormones, including sex hormones, insulin, and insulin-like growth factors, or immune function (2, 8).

The reduction in breast cancer risk associated with physical activity is mainly based on findings from studies on leisure or recreational physical activity, with stronger associations found in case-control studies than in cohort studies. There are fewer reports on occupational physical activity and breast cancer risk, and only a minority of studies have used a combined measure of recreational and occupational physical activity (total activity) with inconclusive results (9-17). The lack of a clear risk pattern may be due to differences in the assessment and definitions of physical activities used across studies; frequency, intensity, and duration of activity have not been systematically examined in all studies, often because of measurement errors in the physical activity assessment methods. A dose-response relation was especially observed in case-control studies and supported by cohort studies where metabolic equivalent (MET) hours per week were applied (18).

In this study, we examine the association of breast cancer risk in premenopausal and postmenopausal breast cancer with various physical activity measures using physical activity variables based on MET values. A secondary aim is to evaluate whether these associations are modified by other potential risk factors.

Materials and Methods

The European Prospective Investigation into Cancer and Nutrition (EPIC) is a multicenter prospective cohort study designed primarily to investigate the association between nutrition and cancer. The EPIC cohort consists of 23 subcohorts in 10 European countries, Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden, and the United Kingdom, thereby allowing comparisons of lifestyle and food habits among regions with very different cancer rates. Food-related and lifestyle questionnaires were administered and anthropometric measurements obtained from all participants at the time of enrollment (1992-2000). The 366,521 eligible female participants were mostly of ages 25 to 70 years and recruited from the general population residing in a given geographic area, such as a town or a province (19). Exceptions were the French cohort (based on female members of the health insurance for school employees), the Utrecht cohort in the Netherlands (based on women attending breast cancer screening), the Ragusa cohort in Italy (based on blood donors and their spouses), and part of the Oxford cohort in the United Kingdom (based on vegetarian volunteers and healthy eaters). Eligible subjects were invited to participate in the study, and those who accepted gave informed consent and completed questionnaires on their diet, lifestyle, and medical history. Study subjects were then invited to a center to provide a blood sample and to have anthropometric measurements taken, methods of which have been reported in full elsewhere (19, 20).

Study Population. The present study was based on data from 335,625 female participants after a priori excluding women with prevalent cancer at any site at baseline examination, those with missing dietary or nondietary questionnaire data, and those who were in the top or bottom 1% of the ratio of energy intake to estimated energy requirement (calculated from age and body weight) to reduce the effect on the analysis of implausible extreme values (21). Women from the Norwegian cohort (n = 35,956) and the cohort from Umeå, Sweden (n = 12,519), were excluded because of lack of data on physical activity. Women were classified according to menopausal status at enrollment based on an algorithm as described elsewhere (22). The study population was further restricted to women who were premenopausal (33.3%) and naturally postmenopausal at recruitment (48.1%), thus excluding perimenopausal women (15.0%) or those who had undergone surgical menopause (3.6%). The analytic cohort for this study therefore consisted of 218,169 women from nine countries, of whom 90,060 were premenopausal and 128,109 were postmenopausal. The present analysis included some women from the French E3N study published in 2006 (23). However, in that study, the findings were based on physical activity data derived from the baseline questionnaire of the E3N study. These physical activity questions were different from the EPIC core questions that were added later in the third questionnaire of the E3N cohort and used in this analysis.

End Points and Ascertainment of Cases. Incident breast cancer cases were identified through population cancer registries (Denmark, Italy, Netherlands, Spain, Sweden, and United Kingdom) or by active follow-up (France, Germany, and Greece), depending on the follow-up systems in each of the participating countries. The active follow-up procedure used a combination of methods including health insurance records, cancer and pathology registries, and via contact with participants and their next-of-kin. Women were followed from study entry (1992-2000) until first breast cancer diagnosis, death, emigration, or end of the follow-up period. By January 2005, 5,763 breast cancer cases had been reported to the common data base at the IARC, Lyon, based on information on complete follow-up data up until December 2001 or December 2002 in most of the centers. Mortality data were coded according to the 10th Revision of the International Statistical Classification of Diseases, Injuries, and Causes of Death (ICD-10), and cancer incidence data were coded according to ICD-O-2. This analysis included 3,423 invasive (primary, malignant) breast cancer cases, of which 869 occurred in women who were premenopausal at recruitment and 2,554 in postmenopausal women.

Classification of Physical Activity Measures and Other Predictor Variables. The physical activity assessment used in the EPIC study has previously been described (24, 25). An assessment of the relative validity and reproducibility of the nonoccupational physical activity questions was undertaken in a sample of men and women from the Netherlands and the questionnaire was found to be satisfactory for the ranking of subjects although it was less suitable for the estimation of energy expenditure (26).

Physical activity data were obtained using in-person interviews or via a self-administered standardized questionnaire (24). Data on current occupational activity included employment status and the level of physical activity done at work (nonworker, sedentary, standing, manual, heavy manual, and unknown). Information on the frequency and duration of nonoccupational physical activity during the past year included housework (such as cleaning, washing, cooking, child care, etc.), home repair (do-it-yourself activities), gardening, stair climbing, and recreational activities (walking, cycling, and all other sports combined as done in winter and summer separately) and vigorous physical activity. Housework, home repair, gardening, and stair climbing were combined to obtain an overall estimate of household activity. Walking (including walking to work, shopping, and leisure time), cycling (including cycling to work, shopping, and leisure time), and sports activities were combined to derive overall recreational activity. Because the intensity of recreational and household activities was not

directly recorded, a MET value was assigned to each reported activity according to the *Compendium of Physical Activities* (27). A MET is defined as the ratio of work metabolic rate to a standard metabolic rate of 1.0 (4.184 kJ)·kg^{-1}·h^{-1}. The MET values assigned to the nonoccupational data were 3.0 for walking, 6.0 for cycling, 4.0 for gardening, 6.0 for sports, 4.5 for home repair (do-it-yourself work), 3.0 for housework, and 8.0 for stair climbing. These mean MET values were obtained by estimating the average of all comparable activities in the *Compendium*. The mean numbers of hours per week of summer and winter household and recreational activities were estimated and then multiplied by the appropriate MET values to obtain MET-hours per week of activity. Vigorous physical activity when reported as practiced (yes/no; ref. 24) was also expressed as MET-hours per week after assignment of a MET value of 9 to the reported hours of vigorous physical activity.

To derive an estimate of total physical activity, household and recreational activities were combined in MET-hours per week and divided into quartiles (low, medium, high, and very high) and cross-classified with the categories of occupational activity. This total activity index was categorized as ''inactive,'' ''moderately inactive,'' ''moderately active,'' and ''active''; the cross-classification is presented in Appendix 1.

Information on reproductive, sociodemographic, and lifestyle characteristics was obtained from the standardized questionnaire at study entry. Body measures were self-reported or assessed during a physical examination at study entry (28). Other known risk factors included in this analysis were age at menarche (≤11, 12-15, >15 years), age at first pregnancy (first birth <20, 20-30, >30 years, nulliparous), education (none/primary school, technical/professional school, secondary school, university), smoking status (never, former, current), alcohol consumption as grams of ethanol per day (abstainers, 1-14, 15-30, >30 g/d), body mass index (BMI; continuous), current oral contraceptive use (no/yes), and current hormone replacement therapy (HRT) use (no/yes). Current hormone use refers to the use of menopausal hormones at the time of recruitment as derived from the country-specific questionnaires or during interviews and includes estrogen alone and combined estrogen/progestin preparations (referred to as HRT use).

Statistical Analysis. Cox proportional hazards models were used to estimate adjusted hazard ratios (HR) and 95% confidence intervals (95% CI) of breast cancer incidence for each physical activity measure for premenopausal and postmenopausal women separately. Age was used as the underlying (primary dependent) time variable in the counting process formulation with entry time t_0 defined as the subject's age at recruitment, and exit time t_1 defined as the subject's age at breast cancer diagnosis or censoring date. All multivariate models were stratified by age at recruitment and by study center to be less sensitive against violations of the proportional hazards assumption, and simultaneously adjusted for the following established or potential breast cancer risk factors: BMI, age at menarche, age at first pregnancy, education, smoking status, alcohol consumption, current oral contraceptive use, and current HRT use. Estimated energy intake was derived from the food frequency questionnaire data applied in the EPIC study (19) and used as covariate in subanalyses. An indicator category for missing responses for each covariate was created to minimize the loss of observations due to missing covariate data.

Trend tests were calculated for quartile-based or category-based scores, assigning a score from 1 to 4 to an individual according to the interquartile interval of the selected physical activity measure. For country-specific analyses, physical activity measures with assigned MET scores were treated as continuous variables. To estimate the overall effect across countries, the method of DerSimonian and Laird (29), based on the random effects model, was used. Heterogeneity between country-specific risk ratios was assessed by Cochran's χ^2 test (30).

Potential effect modifications of the physical activity-breast cancer association were examined by (*a*) BMI (continuous), (*b*) alcohol intake (continuous), and (*c*) current HRT use (yes/no in postmenopausal women only). A P value for interaction was estimated for the interaction term of the test variable and the physical activity trend variable (quartile- or category-based score) over the entire cohort of premenopausal or postmenopausal women. All tests of statistical significance were two sided and $P < 0.05$ was considered statistically significant. The statistical analyses were done with the use of the PHREG procedure in the Statistical Analysis System (SAS) software package, version 9 (SAS Institute, Cary, NC).

Results

The analytic cohort of 218,169 women, ages 20 to 80 years at baseline, was followed since 1992 for an average period of 6.4 (±1.8) years, yielding a total of 1,400,935 person-years. Table 1 provides the cohort characteristics of the female participants stratified by menopausal status. The median age at breast cancer diagnosis was 47.6 years for premenopausal women and 65.6 years for postmenopausal women.

Table 1. Cohort characteristics by menopausal status, the EPIC study

Country	Premenopausal				Postmenopausal			
	Cohort size (*n*)	Age, baseline median (range)	Person-years	No. cases*	Cohort size (*n*)	Age, baseline median (range)	Person-years	No. cases*
France	12,429	46 (42-58)	104,968	266	28,829	58 (43-71)	238,066	773
Italy	10,879	43 (29-58)	67,534	156	12,580	57 (39-78)	75,986	209
Spain	13,100	42 (29-57)	86,192	106	7,888	58 (40-70)	51,708	86
United Kingdom †	25,582	36 (20-58)	138,865	135	18,371	61 (39-80)	99,134	289
The Netherlands	8,603	38 (20-58)	46,238	75	12,701	59 (39-70)	92,636	273
Greece	5,384	40 (20-57)	20,155	11	7,656	63 (40-80)	28,424	26
Germany	12,006	40 (20-58)	69,182	69	10,499	58 (39-70)	61,412	163
Sweden ‡	—	—	—	—	9,635	61 (45-74)	73,455	232
Denmark	2,077	52 (50-58)	13,670	51	19,950	58 (50-66)	133,304	503
Total	90,060	42 (20-58)	546,807	869	128,109	59 (39-80)	854,127	2,554

*Invasive (malignant, primary) breast cancer.
†The United Kingdom cohort consists of participants recruited from both the general population (n = 12,984) and health-conscious individuals (i.e., vegetarians and healthy eaters; n = 30,969).
‡Sweden: data presented are based on the Malmö cohort; data on premenopausal women not available.

Characteristics of the study population stratified by case status are presented in Table 2. Compared with noncases, cases were older at study entry and tended to be older at their first birth. Cases were also less likely to be nulliparous and to currently use oral contraceptives, but more likely to be current HRT users and high alcohol consumers. Overall, 16% of all women were classified as physically inactive. Cases were more likely to be ''moderately inactive'' or ''inactive'' than noncases. The lower activity level among cases was also reflected in the mean MET-hours per week for recreational and household activities. Other characteristics, such as age at menarche, educational attainment, and smoking status, were similar between cases and noncases.

Because the magnitude of the associations for physical activity and breast cancer risk usually observed in previous studies has differed by menopausal status, the associations by type of physical activity and risk of breast cancer among premenopausal and postmenopausal women were examined separately (Table 3). For total physical activity (i.e., combined occupational, recreational, and household activities), increasing activity level was associated with an overall decrease in breast cancer risk in postmenopausal women only, although the trend in the multivariate-adjusted analysis did not reach statistical significance. There was no significant association between total physical activity and breast cancer risk in premenopausal women. Occupational activity was unrelated to risk of breast cancer in all women.

Stronger and significant risk reductions became apparent for combined recreational and household activities and for household activity alone. Among postmenopausal women, compared with women in the lowest quartile of combined recreational and household activities, women in the top quartile had a 17% reduced risk of breast cancer after adjusting for multiple covariates. A similar risk reduction was observed in premenopausal women, but none of the individual categorical risk estimates reached statistical significance when adjusted for other risk factors. Household activity on its own was significantly inversely related to breast cancer risk in premenopausal and postmenopausal women; the HRs for the highest versus the lowest quartile of household activity were 0.71 (95% CI, 0.55-0.90) for premenopausal women and 0.81 (95% CI, 0.70-0.93) for postmenopausal women. Recreational activity alone was not significantly associated with risk.

In additional analyses, mutual adjustment of recreational, household, and occupational activities did not materially affect the risk estimates in the respective physical activity models in either premenopausal or postmenopausal women (data not shown). Finally, additional adjustment for energy intake or the omission of BMI in the different models did not alter any of the HRs (data not shown).

The individual activities, housework, home repair, gardening, stair climbing, walking, cycling, and sports activities, in MET-hours per week, were each inversely associated with breast cancer risk with nonsignificant trends, except for housework (P_{trend} = 0.002, premenopausal women; P_{trend} = 0.016, postmenopausal women) and sports activities (P_{trend} = 0.01, postmenopausal women). Housework was the predominant component of household activity. On average, premenopausal women spent a mean (SD) of 17.7 (14.3) h and postmenopausal women 16.1 (13.2) h on housework chores. Vigorous activity, defined as MET-hours per week, was not significantly associated with breast cancer risk in either of the menopausal groups. Overall, <40% of all women engaged in vigorous activity (data not shown).

Figure 1 shows the multivariate adjusted risk estimates for breast cancer in relation to continuous household activity by 20 MET-h/wk for all cohorts combined and for individual countries with at least 50 cases of breast cancer, stratified by menopausal status. An increase of one increment of household activity (20 MET-h/wk) was associated with a pooled HR of 0.97 (95% CI, 0.94-0.99; P = 0.008) in postmenopausal women and 0.96 (95% CI, 0.92-1.00; P = 0.06) in premenopausal women. No evidence of heterogeneity between countries was present for this and any other of the presented analyses, except for recreational activity among postmenopausal women ($P_{heterogeneity}$ = 0.02).

We assessed the potential effect modification by BMI, current alcohol consumption, and current HRT use in postmenopausal women, conducting stratified analyses. Formal testing did not reveal any statistically significant interactions between each of these factors and any of the physical activity measures, although the inverse association between total activity level and breast cancer risk in postmenopausal women tended to be strongest in lean women (BMI <25; P_{trend} = 0.07) compared with overweight or obese women (data not shown).

Table 2. Sociodemographic and lifestyle characteristics by case-status; the EPIC study

Characteristic	Cases (n = 3,423)	Noncases (n = 214,746)
	Mean (SD)	
Age at enrollment (y)	55.6 (7.7)	51.5 (11.3)
BMI (kg/m^2)	25.0 (4.4)	25.1 (4.5)
Recreational activity (MET-h/wk)	30.0 (24.1)	31.1 (24.9)
Household activity (MET-h/wk)	54.3 (41.1)	62.7 (43.8)
	%*	
Age at menarche (y)		
<8-11	13.6	15.2
12-14	70.0	67.6
15+	15.8	16.2
Age at first pregnancy (y)		
<20	4.4	6.0
20-30	65.6	62.7
>30	13.5	11.7
Nulliparous	13.5	17.3
Education		
Primary school or less	25.5	27.6
Technical school	19.7	20.7
Secondary school	28.1	24.2
University degree	21.8	22.8
Alcohol consumption (g/d)		
Nondrinker	13.6	16.3
0-15	63.2	65.8
15-30	13.9	11.9
>30	9.2	6.0
Smoking status		
Never smokers	57.5	58.6
Former smokers	24.5	21.9
Current smokers	16.9	18.2
Current HRT use†		
Yes	39.0	25.4
Current oral contraceptive use‡		
Yes	3.5	11.6
Total physical activity		
Inactive	17.5	15.8
Moderately inactive	42.2	36.5
Moderately active	33.2	39.3
Active	6.5	7.3
Occupational activity		
Sedentary	22.4	23.9
Standing	24.1	23.1
Manual and heavy manual	8.2	6.9
Nonworker	42.0	43.1

*Numbers within each stratum do not add up to 100% due to missing values.
†Postmenopausal women.
‡Premenopausal women.

Discussion

In this large cohort of women from nine European countries, ages 20 to 80 years at study enrollment, increased

Table 3. Crude and multivariate-adjusted HRs of breast cancer in 218,169 women according to type of physical activity, stratified by menopausal status; the EPIC study

Type of physical activity	Premenopausal women (n = 90,060)			Postmenopausal women (n = 128,109)		
	Cases*	HR† (95% CI)	HR‡ (95% CI)	Cases*	HR† (95% CI)	HR† (95% CI)
Total activity index§						
Inactive	171	1.0 (1.0)	1.0	382	1.0	
Moderately inactive	331	1.02 (0.85-1.23)	1.02 (0.84-1.24)	1,058	0.87 (0.77-0.98)	0.89 (0.79-1.00)
Moderately active	245	0.82 (0.66-0.99)	0.84 (0.68-1.04)	885	0.80 (0.71-0.91)	0.84 (0.74-0.96)
Active	73	0.98 (0.72-1.25)	1.02 (0.77-1.36)	151	0.87 (0.71-1.05)	0.92 (0.76-1.12)
P_{trend}		0.187	0.267		0.007	0.06
Occupational activity‖						
Sedentary	274	1.0	1.0	495	1.0	1.0
Standing	322	1.01 (0.84-1.20)	1.02 (0.86-1.22)	514	0.91 (0.79-1.03)	0.92 (0.81-1.05)
Manual and heavy manual	63	0.98 (0.74-1.31)	1.04 (0.78-1.38)	216	1.05 (0.89-1.24)	1.08 (0.91-1.29)
P_{trend}		0.954	0.771		0.942	0.743
Combined recreational and household activities¶ (MET-h/wk)						
<55	259	1.0	1.0	788	1.0	1.0
55-85	209	0.91 (0.76-1.10)	0.92 (0.76-1.10)	703	0.94 (0.84-1.04)	0.94 (0.85-1.05)
86-126	202	0.89 (0.73-1.09)	0.91 (0.74-1.11)	566	0.84 (0.75-0.94)	0.86 (0.76-0.96)
>126	186	0.80 (0.64-0.99)	0.82 (0.66-1.03)	490	0.81 (0.71-0.92)	0.83 (0.73-0.95)
P_{trend}		0.047	0.107		0.0003	0.002
Recreational activity¶ (MET-h/wk)						
<14	226	1.0	1.0	652	1.0	1.0
14-24	226	0.91 (0.76-1.10)	0.91 (0.75-1.10)	692	1.06 (0.95-1.18)	1.05 (0.94-1.17)
25-42	218	0.96 (0.79-1.15)	0.95 (0.78-1.14)	624	0.93 (0.84-1.04)	0.92 (0.83-1.03)
>42	186	0.95 (0.77-1.16)	0.94 (0.76-1.15)	579	0.95 (0.85-1.07)	0.96 (0.85-1.08)
P_{trend}		0.666	0.580		0.157	0.176
Household activity¶ (MET-h/wk)						
<28	252	1.0	1.0	767	1.0	1.0
28-52	233	0.92 (0.76-1.10)	0.92 (0.77-1.11)	709	0.92 (0.83-1.02)	0.94 (0.85-1.04)
53-90	194	0.80 (0.65-0.97)	0.80 (0.65-0.99)	613	0.84 (0.75-0.95)	0.86 (0.76-0.96)
>90	177	0.68 (0.54-0.86)	0.71 (0.55-0.90)	458	0.78 (0.68-0.89)	0.81 (0.70-0.93)
P_{trend}		0.0007	0.003		0.0001	0.001

*Numbers of cases do not always add up to total number of cases across each physical activity variable due to some missing values.
†Crude relative risks: stratified by age at recruitment and study center (Cox model using age as underlying time variable).
‡Multivariate relative risks: based on crude model and additionally adjusted for educational attainment, smoking status, alcohol consumption, BMI, age at menarche, age at first pregnancy, current oral contraceptive use (premenopausal), and current HRT use (postmenopausal).
§Combined total physical activity index that is categorized into four activity levels based on a cross-tabulation of occupational activity by the combined household and recreational activities.
‖Categorical variable based on type of physical activity at work; nonworking category and missing values were excluded; manual and heavy manual categories were collapsed into one category due to low number of subjects; total premenopausal cases n = 659, postmenopausal cases n = 1,225.
¶Quartile cut points were obtained from the combined premenopausal and postmenopausal analytic cohort.

nonoccupational physical activity and, in particular, increased household activity were significantly associated with reduced breast cancer risk, independent of other potential risk factors. These results strengthen the consistency of findings about the protective role of physical activity on breast cancer risk (2, 7).

Our results, based on a large and heterogeneous cohort and which used standardized data collection of physical activity and that could control for all the potential confounding factors, provide additional evidence that moderate forms of physical activity, such as household activity, may be more important than less frequent but more intense recreational physical activity in reducing breast cancer risk in European women.

This study has some limitations that need to be considered when reviewing these results. Although the data collection was standardized across the nine countries included in this analysis, data were only available on past year physical activity (24), and thus the effect of physical activity in different time periods of life on breast cancer risk could not be examined. In addition, there were no data available on the frequency, duration, and specific intensities of occupational activity; hence, only categories of occupational activity were recorded. Furthermore, there were few study participants who were categorized in manual and heavy manual occupations, thereby limiting the assessment of the effect of intense occupational activity on breast cancer risk. Finally, some misclassification of physical activity levels is likely in this study thereby introducing nondifferential misclassification bias that would have biased the results towards the null.

Despite these limitations, we were able to show a reduction in breast cancer risk for household activity, one of the main sources of physical activity for women in most developed countries (31). These results are in concordance with some (23, 32, 33), but not all (16, 17, 34) studies that have assessed household activity and breast cancer risk. In the Canadian population–based case-control study by Friedenreich et al. (32), which assessed lifetime physical activity, the greatest risk reductions were found for occupational and household activities, specifically among postmenopausal women. Among these women, the breast cancer risk (odds ratio) for the highest quartile of household activity, expressed as MET values, was 0.57 (95% CI, 0.41, 0.79). In our study, the protective effect of household activity was found in both premenopausal and postmenopausal women with risk reductions somewhat smaller than in the Canadian study (32). The assessment of lifetime activity might provide a more accurate, complete assessment of household activity and decrease the amount of measurement error in the assessment that would result in an increase in the effect size.

Household activity (MET-hours per week) during the age period of 12 to 30 years, however, was not related to breast cancer risk in a case-control study of German premenopausal

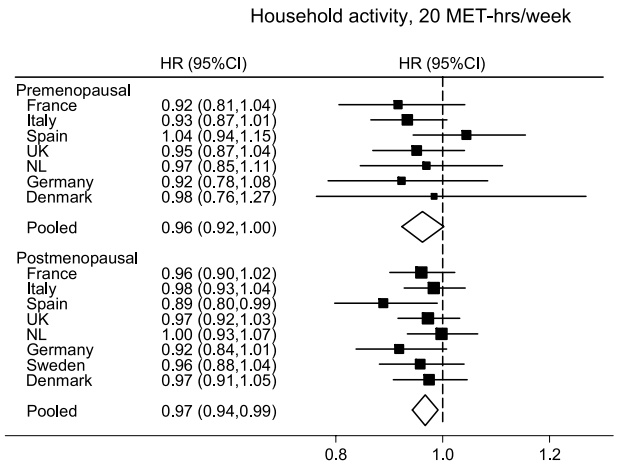

Figure 1. Country-specific and pooled multivariate adjusted HR of breast cancer by menopausal status for household activity (MET-hours per week). Country-specific risk estimates are only presented for countries with ≥50 cases.

women with cases diagnosed under age 51 years (17). Hours of household activity included in the lifetime physical assessment in two case-control studies from the United States (16) and China (34) were not associated with breast cancer risk when adjusted for other risk factors. Yet, in the French E3N cohort study, women who reported ≥14 weekly hours of light household activity had a nonsignificant decreased risk (risk ratio, 0.82; 95% CI, 0.61-1.11) compared with women who had no such activity (23). Differences in study design and physical assessment methods may account for these equivocal findings, as well as for the different magnitude of the observed risk reductions.

Although there is substantial evidence that physical activity is associated with a reduction in breast cancer risk, the associations between occupational and nonoccupational activities are inconsistent (7). The lack of association with work-related activity and breast cancer risk in our study may be, in part, explained by the low number of female subjects in the active categories. Moreover, the association seen with total and nonoccupational physical activity was largely due to household activity and not recreational activity. A similar finding was reported from a study on physical activity and mortality (35). To date, few studies that have assessed total activity and household activity as important source of total activity have rarely been included (6, 31, 36).

The lack of association for recreational activity in our study is corroborated by findings from the Nurses' Health Study indicating no reduction in premenopausal breast cancer risk by recent total recreational activity composed of eight MET value–based activity variables (37), but contrasts with results from the CPS-II Nutrition Cohort (38) that found a significant reduction in risk with increasing recreational activity (MET-hours per week, seven single activities) in postmenopausal women. It is possible that the low prevalence of women engaged in frequent more vigorous recreational activity precluded seeing an effect of recreational activity on breast cancer risk in this study population. In contrast, household activity, which is the main type of physical activity in these women, was associated with a reduced risk in both premenopausal and postmenopausal women and may suggest that more moderate forms of activity are effective in reducing the risk of breast cancer. Other studies have also found risk reductions at moderate intensity levels (13, 16, 33, 39), suggesting that benefits of physical activity may be realized already at these lower intensity levels.

It has not been fully established whether or not the physical activity-breast cancer association is modified by other risk factors, such as body mass, alcohol consumption, or HRT use. Similar to our observation, a somewhat stronger effect of physical activity among lean women has been shown in some (11, 13, 40, 41), but not all, previous studies (16, 17, 34, 42, 43). The biological rationale for a stronger effect of physical activity among lean women has not been established; however, because obesity is a clear risk factor for postmenopausal breast cancer, it is plausible that activity may have a more pronounced effect among lean women (11, 13). We found no evidence that HRT use by postmenopausal women modified the association between physical activity and breast cancer risk, which is in line with several other studies (23, 32, 41, 43, 44), but is in contrast with another (38), which found a stronger association between recreational physical activity and breast cancer risk among non-HRT users. Subgroup analyses in our study did not reveal any effect modification of physical activity on breast cancer risk for alcohol consumption. Findings from the case-control study by Friedenreich et al. (32) indicate that physical activity may have a greater effect for women who are alcohol abstainers, but this effect was not evident in another previous study (38).

In conclusion, this large European study provides additional epidemiologic evidence that increasing physical activity reduces breast cancer risk. The finding that increased household activity reduces the risk warrants further confirmation, but underscores the importance of more moderate types of activities for the prevention of breast cancer among middle-aged and older women. Future cohort studies that have more detailed measures of activity obtained over lifetime will provide further insights into the nature of this association.

Appendix 1. Total Physical Activity Index as the cross-classification of occupational and combined recreational and household activities

Occupational activity	Recreational and household activities (MET-h/wk in quartiles*)			
	Low	Medium	High	Very high
	≤55.0	>55.0-≤85.0	>85.0-≤126.0	>126.0
Sedentary	Inactive	Inactive	Moderately inactive	Moderately active
Standing	Moderately inactive	Moderately inactive	Moderately active	Active
Manual	Moderately active	Moderately active	Active	Active
Heavy manual	Moderately active	Moderately active	Active	Active
Nonworker	Moderately inactive	Moderately inactive	Moderately active	Moderately active

*Based on premenopausal and postmenopausal women.

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