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Vigorous physical activity and risk of breast cancer in the African American breast cancer epidemiology and risk consortium

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Abstract

The relationship between physical activity and breast cancer risk has been extensively studied among women of European descent, with most studies reporting inverse associations. However, data on American women of African ancestry (AA) and by tumor subtypes are sparse. Thus, we examined associations of vigorous exercise and breast cancer risk overall, and by estrogen receptor (ER) status, in the African American Breast Cancer Epidemiology and Risk Consortium. We pooled data from four large studies on 2482 ER+ cases, 1374 ER− cases, and 16,959 controls. Multivariable logistic regression was used to compute odds ratios (OR) and 95 % confidence intervals (CI) for the risk of breast cancer overall, and polytomous logistic regression was used to model the risk of ER+ and ER− cancer. Recent vigorous exercise was associated with a statistically significant, modestly decreased risk for breast cancer overall (OR 0.88, 95 % CI 0.81–0.96) and for ER+ cancer (OR 0.88, 95 % CI 0.80–0.98), but not for ER− cancer (OR 0.93, 95 % CI 0.82–1.06). Overall, there was no strong evidence of effect modification by age, menopausal status, body mass index, and parity. However, our data were suggestive of modification by family history, such that an inverse association was present among women without a family history but not among those with a relative affected by breast cancer. Results from this large pooled analysis

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provide evidence that vigorous physical activity is associated with a modestly reduced risk of breast cancer in AA women, specifically ER+ cancer.

Keywords

Vigorous physical activity; Breast cancer; Subtype; African American women

Introduction

Breast cancer remains the most common cancer and the second leading cause of cancer death in US. women [1]. American women of African ancestry (AA) are more likely than women of European ancestry (EA) to be diagnosed with breast cancer at younger ages, to have more aggressive estrogen receptor (ER)-negative cancers, and to die from breast cancer [2]. There has been a considerable amount of research in identifying risk factors for breast cancer, but most of the established risk factors, such as age, family history of breast cancer, genetic susceptibility, benign breast disease, early menarche and late menopause [3], are not modifiable. Physical activity is amenable to change and, therefore, represents an opportunity to reduce the burden of breast cancer, especially among AA women, who have been found to meet recommendations for physical activity less frequently compared with EA women [4, 5].

Numerous studies over the past two decades, mostly among EA women, have examined the association between physical activity and breast cancer risk. Although findings have been mixed, especially from cohort studies, previous, and recent reviews, including the 2007 World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) report and the 2010 WCRF/AICR Continuous Update, have generally concluded that the evidence is “convincing” [6, 7] or at least “probable” [8, 9] for an inverse association between physical activity and breast cancer risk in postmenopausal women. The evidence in premenopausal women has been limited and generally weaker [7–9]. Many aspects regarding the physical activity breast cancer association remain unclear. Results on whether associations differ according to subtype of breast cancer have been conflicting, but several large studies have found strong associations for ER+ cancer [10–12]. Inconsistencies also remain regarding modifying effects of other risk factors, such as family history of breast cancer, body mass index (BMI), and reproductive factors. Insofar as most studies have focused primarily on EA women, data on physical activity and breast cancer, especially by subtype, are needed for AA women [7].

In this study, we investigated the role of recent physical activity in the risk of breast cancer overall and by tumor ER status in AA women, using data from a large project, the African American Breast Cancer Epidemiology and Risk (AMBER) Consortium. We also examined whether these associations differed by age, menopausal status, family history, BMI, and parity.

Materials and methods

Study population

The AMBER Consortium, a collaborative project of four studies, the Black Women's Health Study (BWHS), the Multiethnic Cohort Study (MEC), the Carolina Breast Cancer Study CBCS), and the Women's Circle of Health Study (WCHS), was formed in 2011 and designed to advance understanding of the determinants of breast cancer risk in AA women, with details described previously [13–17]. Briefly, the BWHS is an ongoing prospective cohort study, with AA women across the US. enrolled in 1995 and then followed every two years through mailed questionnaires. Breast cancer cases are identified by self-report or through linkage with state cancer registries. The MEC is also a prospective cohort study that began in 1993, with participants recruited from Hawaii and Southern California, with AAs primarily from California; cases are identified by linkage to the Hawaii Tumor Registry, the Cancer Surveillance Program for Los Angeles County and the California State Cancer Registry. Each cohort study created nested case-control studies sets that included incident breast cancer cases together with controls frequency matched to the cases by five-year age category; data were taken from questionnaires completed prior to case diagnosis (index date). CBCS, in the first two phases (CBCS 1 & 2), conducted with population-based sampling and in-person interviews in North Carolina from 1993 to 2001. CBCS 3 is ongoing and includes cases only, thus is not included in this analysis. Breast cancer cases in CBCS were identified through the North Carolina Central Cancer Registry by rapid case ascertainment, with oversampling of younger cases. Controls enrolled in CBCS 1 and 2 were identified from Division of Motor Vehicle lists (age <65 years) and from Health Care Financing Administration lists (age 65 years or older). The WCHS is a case-control study that started in New York City (NYC) and currently recruits AA women in New Jersey (NJ) only. Breast cancer cases were identified using hospital-based case ascertainment in targeted hospitals in the NYC area from 2002 to 2008 and by population-based rapid case ascertainment in NJ since 2006 through the NJ State Cancer Registry. Controls were identified through random digit dialing and supplemented by community-based recruitment efforts [18]. Pooled data from the four studies resulted in a total of 4416 invasive breast cancer cases and 16,959 controls after exclusion of women with missing values for vigorous physical activity ($n = 606$).

Data collection

Information including demographic factors, family history of breast cancer, reproductive and medical history, hormone use, lifestyle factors, and weight and height were collected at baseline and updated every two years for BWHS and every five years for MEC by mail questionnaire. Data for these factors were collected in CBCS and WCHS by in-person interviews. Immunohistochemistry results of breast cancer were obtained from hospital pathology records and cancer registry data, and were used to classify cases as ER+ and ER− breast cancer. Each study was approved by the relevant Institutional Review Boards and obtained informed consent from all participants. Data on key variables from each study were harmonized at the coordinating center. Many of the variables (e.g., age, education, family history, body mass index, and female hormone use) were asked in these studies using similar questions. For some variables (e.g., age at first birth, age at menopause), categories were collapsed so as to have categories common to all the studies. For variables in which there was some question as to how to harmonize the variable (e.g., physical activity), the study investigators, with the data coordinating center staff, discussed and mutually agreed upon the most appropriate categorization (see below).

Vigorous recreational physical activity

We harmonized data on recent vigorous recreational physical activity as follows. In BWHS, participants were asked to report the average number of hours per week they spent on vigorous activity (e.g., basketball, bicycling on hills, running, swimming, and aerobics). Response options were 0, <1, 1, 2, 3–4, 5–6, 7–9, and 10+ h/week. In MEC, participants reported their average hours per week spent on vigorous exercise (e.g., jogging, bicycling on hills, tennis, racquetball, swimming laps, and aerobics) in categories of never, ½ to 1, 2–3, 4–6, 7–10, 11–20, 21–30, and 31+ h/ week. In CBCS 1 and 2, participants were asked to report activities that they engaged in regularly on a weekly basis to keep them physically fit and to describe how often they participated in that activity. The response options were 1) daily (7 days); 2) several times (5–6 times); 3) every other day (3–4 times); and 4) once or twice (1–2 times) a week. We then converted the number of days of activity (using the lowest number of days in the range) to hours per week by assuming that participants engaged in an average of 45 min of the reported activity each day. This assumption was based on comparisons of the distributions of activity patterns in CBCS 1 and 2 with data collected in CBCS 3, which collected continuous measures of vigorous physical activity. A sensitivity analysis was performed to test the impact of these assumptions. In WCHS, participants reported any activities they participated in for at least one hour per week for at least three months. A metabolic equivalent of energy expenditure (MET) value was assigned to each reported activity according to the Compendium of Physical Activity [19, 20]. Participants were asked to report any activities they engaged in, and data were recorded on the type of activity, the number of years in total for the activity, the number of months per year, and the average hours per week. Average hours per week were then computed for vigorous activity, defined as activities with a MET value of 6.0 or greater. We assessed various categorizations of physical activity, including 0, <2, 2–6, and 7+ h/week, and due to small numbers (n = 86 cases) in the 7+ category, categories were further collapsed down to 0, <2, and 2+ h/week in models examining potential effect modification by several breast cancer risk factors.

Statistical analysis

Multivariable unconditional logistic regression was used to estimate odds ratios (ORs) and 95 % confidence intervals (CIs) for the association between vigorous activity and risk of breast cancer. The potential confounding factors included in the multivariable models were age (continuous), study (BWHS, MEC, CBCS, WCHS), geographic region (South, Midwest, West, New Jersey, other Northeast), time period (1993–98, 1999–2005, 2006–2014), education (<12, 12, 13–15, 16, >16 years), first-degree family history of breast cancer (yes, no), age at menarche (<11, 11–12, 13–14, 15–16, ≥17 years), BMI (<18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, 35–39.9, and 40+ kg/ m^2), menopausal status and age at menopause (pre-menopausal, ages <45, 45–49, 50–54, or ≥55 years, or menopausal status undetermined), parity (0, 1, 2, 3, 4, 5, 6, ≥7), cigarette smoking (0, <10, 10–19, ≥20 pack years), alcohol consumption (never, past drinkers, current drinkers at <1, 1–3, 4–6, 7–13, 13–20, 21+ drinks per week), and female hormone use (ever, never). Women who reported no vigorous activity were used as the referent group. Polytomous logistic regression models were used for examining the associations for ER+ and ER− breast cancer. In addition to the case-control analyses, case-case analyses were performed to estimate ORs for the association of vigorous physical activity to ER− relative to ER+ breast cancer.

Tests for a linear trend across categories of hours per week of vigorous physical activity were done using an ordinal variable corresponding to rank from lowest to highest category, as described by Breslow and Day [21]. To test whether the association between vigorous activity and breast cancer risk was modified by other factors, we performed the likelihood ratio test by comparing two multivariable-adjusted logistic regression models. We examined effect modification by age (<50 years vs ≥50 years), menopausal status (premenopausal versus postmenopausal), first-degree family history of breast cancer (yes vs no), BMI (<30 kg/m^2 vs ≥30 kg/m^2), and parity (nulliparous vs parous). In addition, heterogeneity between studies was tested using Cochran's Q statistic. A sensitivity analysis was also performed to evaluate the impact of our assumptions in computing CBCS physical activity variables; specifically, we compared findings from analyses in which CBCS was included to those after exclusion of CBCS.

All analyses were conducted using SAS V9.4 (SAS Institute, Cary, CA). Statistical tests were two-sided and considered statistically significant for $P<0.05$.

Results

Selected characteristics of breast cancer cases and controls are presented in Table 1. Among the 3856 (87.3 %) breast cancer tumors with known ER status, 2482 (64.4 %) were ER+ and 1374 (35.6 %) were ER−, with 32 % of cases diagnosed before age 50. The CBCS, designed to oversample younger AA women, had the highest proportion of ER− breast cancer. In contrast, MEC has an older population and the highest prevalence of ER+ breast cancer. The highest prevalence of engaging in vigorous physical activity was observed in CBCS women, whereas the lowest prevalence was found among WCHS participants. The prevalence of vigorous activity was similar for MEC and BWHS participants.

Associations of recent vigorous physical activity with risk of breast cancer overall and by ER status are presented in Table 2. Overall, women who had engaged in vigorous exercise had a significantly decreased risk of breast cancer (OR 0.88, 95 % CI 0.81–0.96) compared with women who did not engage in any vigorous exercise. There was a statistically significant inverse trend across categories of hours per week of vigorous activity (p trend = 0.007), but there was no clear dose–response relationship. Relative to no vigorous exercise, the ORs were 0.90 (95 % CI 0.81–1.01), 0.88 (95 % CI 0.79–0.98), and 0.86 (95 % CI 0.68–1.10) for the activity categories <2, 2–6, and 7+ h/ week, respectively. For the combined category of >=2 h/ week, the OR was 0.88 (95 % CI 0.79–0.97) (data not shown). In the analysis by ER status, the inverse association associated with vigorous exercise (any vs none) was statistically significant for ER + cancer (OR 0.88, 95 % CI 0.80–0.98), but not for ER− breast cancer (OR 0.93, 95 % CI 0.82–1.06). However, when we compared ER− with

ER+ breast cancer in case–case analyses, there were no significant differences in risk patterns by ER status (Table 2).

We examined whether these associations were modified by age, menopausal status, family history, BMI, and parity. As shown in Table 3 for breast cancer overall, we found no statistically significant interactions for any of these associations in the analysis. However, results suggested that the pattern of association may differ for women with and without a first-degree family history of breast cancer (p interaction = 0.09). The inverse association associated with any vigorous exercise was present among women without a family history (OR 0.86, 95 % CI 0.79–0.94), but not among those with a relative affected by breast cancer (OR 1.04, 95 % CI 0.82–1.30). In addition, a significant inverse association was observed among premenopausal women, those with BMI <30 kg/m^2, parous women, and in women ages <50 and ages >= 50. As shown in Table 4, we found generally similar association patterns for ER+ cancer and total breast cancer. There was suggestive evidence that the association of physical activity with ER+ cancer was modified by family history (p interaction = 0.07).

Statistical tests indicated that there were no significant differences between studies in the meta-analysis (p heterogeneity >0.05). Sensitivity analyses showed that the estimates remained largely the same after exclusion of CBCS participants from the primary analysis (ORs for <2, 2–6, 7 + h/week: 0.93, 0.86, 0.87; data not shown).

Discussion

In this large pooling study of breast cancer in AA women, we observed that any recent vigorous physical activity was associated with a modest, but statistically significant decreased risk of breast cancer, especially ER + cancer, although the difference by ER status was not statistically significant. There was not a clear dose–response relationship of decreasing breast cancer risk with increasing physical activity. In particular, the estimates of association for the categories <2, 2–6, and 7+ were similar. We found no strong evidence that age, menopausal status, BMI, and parity modified the association between recent vigorous physical activity and breast cancer. However, there was suggestive evidence of modification by family history, such that an inverse association was present among women without a family history but not among those with a family history of breast cancer.

Many studies, in populations mostly of EA women, suggest that physical activity is inversely associated with breast cancer risk, with stronger evidence observed in postmenopausal than in premenopausal women [22]. Inverse associations are strongest for vigorous recreational physical activity, as reported in a recent meta-analysis [23]. Data on AA women are limited, with few studies that have specifically examined the association in an AA population or populations that include adequate AA representation [10, 12, 24–29]. High levels of vigorous activity during early adult years or at study baseline were associated with decreased risk of breast cancer in two previous analyses in the BWHS (716 and 1330 AA cases, respectively) [24, 29]. An inverse association was observed for lifetime recreational physical activity in a large case-control study (1605 AA cases) [10], and for lifetime total activity in another study (394 AA cases) [25]; with both studies, finding no differences by menopausal status. Recent recreational physical activity was inversely associated with breast cancer for both pre- and postmenopausal women in two small case-control studies (97 and 88 AA cases, respectively) [26, 27], and for postmenopausal women in another larger study (660 AA cases) [12]. There was no association for recent recreational or other type of physical activity in the Southern Community Cohort, but those results were based on only 313 AA cases [28]. Thus, there is no strong evidence to conclude that an association of physical activity with reduced risk of breast cancer in AA women differs by menopausal status.

Our study of AA women included a large number of ER− breast cancer cases. The inverse association was stronger and statistically significant for ER+ cancer, although the difference by ER status was not statistically significant. Previous studies of physical activity and breast cancer by ER status generally found no statistically significant difference in risk by ER status in pre- or post-menopausal women [11, 26, 29–36]. However, several of the large studies suggested a stronger inverse association for ER+ breast cancer [10–12, 31, 34, 37], including the two studies that conducted analysis by ER status in a larger AA population [10, 12]. In contrast, two studies reported a significant inverse association for ER− breast cancer in postmenopausal women [38, 39]. The observed inverse physical activity-breast cancer association is generally modest, and power from most studies has been limited to detect differences by ER status.

A number of studies have explored whether the physical activity breast cancer association is modified by other risk factors of breast cancer, including age, BMI, family history and parity, with mixed results [22]. In the current study of AA women, there was suggestive evidence that a family history of breast cancer may modify the association between vigorous activity and breast cancer. Several studies [10, 38, 40], although not others [26, 41], have reported similar results as ours that a significant decreased risk of breast cancer was observed among women with no family history of breast cancer and with no risk reduction observed for those with a family history. Several mechanisms by which physical activity could reduce risk of breast cancer have been proposed, including changes in menstrual characteristics, reduction of fat mass, lowering the production and bioavailability of endogenous hormones such as estrogen and insulin, and modulation of chronic inflammation and the immune system [42, 43]. It may be easier to detect a small difference in risk attributable to physical activity among women at lower baseline risk of breast cancer, such as women without a family history. In addition, genetic factors associated with family history may confer a unique susceptibility to hormonal derangements or other underlying mechanisms. Serum concentrations of estradiol and estrone have been shown to be higher in women with a family history of breast cancer [44]. Thus, family history may belie other differences between women that may mediate the effects of physical activity. This also could be explained as limited power due to small sample size of women who had a first-degree family history of breast cancer in these studies.

This study has several strengths. It is the largest study assessing physical activity and risk of breast cancer overall and by tumor subtypes, specifically in AA women. Extensive data were collected on various risk factors, enabling us to adjust for potential confounding and to further examine possible effect modification. However, there are also limitations. Physical activity was self-reported, and data were pooled from four studies with differences in physical activity assessment, which hampered our ability to examine lifetime, other types (e.g., occupational and household activity) or total physical activity. However, we were able to evaluate recent vigorous physical activity, the type of activity most consistently shown to be associated with reduced breast cancer risk [8, 23], and uniformly collected in AMBER. Vigorous-intensity physical activity may be more accurately reported than lower-intensity activities and therefore resulting in less random misclassification. In addition, our assumption about the duration of exercise for CBCS participants was based on data collected in a later phase of CBCS and may have overestimated physical activity levels. Indeed, prevalence of the highest activity levels was greater in CBCS than in all the other studies. However, excluding CBCS did not substantially alter the findings.

In summary, this large study provides further epidemiologic evidence that recent vigorous activity is associated with a decreased risk of breast cancer in AA women. Specifically, two or more hours per week of vigorous activity may be sufficient to reduce risk. It may be more feasible to modify physical activity than to modify obesity, making physical activity a promising target for intervention to reduce the burden of this most common cancer among women.

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Table 1

Characteristics of breast cancer cases and controls by study in the AMBER consortium

	BWHS *N* (%)		MEC *N* (%)		CBCS *N* (%)		WCHS *N* (%)		Total *N* (%)	
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
Total	1744	10785	1051	4167	788	787	833	1220	4416	16959
By ER status										
ER+	956 (54.8)		638 (60.7)		353 (44.8)		535 (64.2)		2482 (56.2)	
ER−	519 (29.8)		228 (21.7)		383 (48.6)		244 (29.3)		1374 (31.1)	
Unknown	269 (15.4)		185 (17.6)		52 (6.6)		54 (6.5)		560 (12.7)	
Age at diagnosis (years)										
<40	143 (8.2)		0		133 (16.9)		108 (13.0)		384 (8.7)	
40–49	510 (29.2)		16 (1.5)		256 (32.5)		238 (28.6)		1020 (23.1)	
50–59	570 (32.7)		168 (16.0)		180 (22.8)		295 (35.4)		1213 (27.5)	
≥60	521 (29.9)		867 (82.5)		219 (27.8)		192 (23.0)		1799 (40.7)	
Recent vigorous physical activity										
No	1285 (73.7)	7513 (69.7)	773 (73.6)	3054 (73.3)	440 (55.8)	415 (52.7)	714 (85.7)	1038 (85.1)	3212 (72.7)	12020 (70.9)
Yes	459 (26.3)	3272 (30.3)	278 (26.4)	1113 (26.7)	348 (44.2)	372 (47.3)	119 (14.3)	182 (14.9)	1204 (27.3)	4939 (29.1)

* *BWHS* Black women's health study, *MEC* Multiethnic cohort, *CBCS* Carolina breast cancer study, *WCHS* Women's circle of health study

Table 2

Vigorous physical activity in the recent past and risk of invasive breast cancer in the AMBER consortium

Vigorous PA	Controls	Total breast cancer		ER-positive		ER-negative		Case-only analyses of ER-negative versus ER-positive cancer
		Cases	OR (95 % CI)[a]	Cases	OR (95 % CI)[a]	Cases	OR (95 % CI)[a]	OR (95 % CI)[a, b]
No	12020	3212	1.00	1834	1.00	957	1.00	1.00
Yes	4939	1204	0.88 (0.81–0.96)	638	0.88 (0.80–0.98)	413	0.93 (0.82–1.06)	1.07 (0.91–1.26)
<2 h/week	2132	476	0.90 (0.81–1.01)	279	0.95 (0.82–1.09)	142	0.89 (0.73–1.07)	0.96 (0.76–1.20)
2–6 h/week	2245	626	0.88 (0.79–0.98)	312	0.85 (0.74–0.97)	247	0.99 (0.84–1.17)	1.18 (0.96–1.45)
7+ h/week	471	86	0.86 (0.68–1.10)	47	0.88 (0.64–1.20)	24	0.85 (0.56–1.30)	0.99 (0.59–1.66)
p trend			0.007		0.02		0.54	0.24

[a]Adjusted for age, study, time period, geographic region, education, age at menarche, parity, alcohol consumption, smoking, body mass index, first-degree family history of breast cancer, menopausal status and age at menopause, and female hormone use

[b]Case-only analysis, OR and 95 % CI represent the odds of ER-negative relative to ER-positive breast cancer

Table 3

Vigorous physical activity in the recent past and risk of invasive breast cancer, stratified by age, menopausal status, family history of breast cancer, body mass index, and parity, in the AMBER consortium

Vigorous PA	Cases/Controls	OR (95 % CI)[a]	Cases/Controls	OR (95 % CI)[a]	*P* interaction
	Premenopause		Postmenopause		
No	996/3429	1.00	2006/7826	1.00	
Yes	449/1963	0.83 (0.72–0.95)	670/2626	0.91 (0.82–1.02)	0.26
<2 h/week	152/769	0.79 (0.65–0.97)	298/1221	0.98 (0.85–1.13)	
2+ h/week	296/1191	0.85 (0.72–1.00)	358/1317	0.88 (0.77–1.02)	
p trend		0.02		0.10	0.34
	Age <50 yrs		Age ≥50 yrs		
No	946/3346	1.00	2266/8674	1.00	
Yes	458/1897	0.85 (0.74–0.98)	746/3042	0.88 (0.80–0.97)	0.67
<2 h/week	144/694	0.87 (0.70–1.07)	332/1438	0.91 (0.79–1.04)	
2+ h/week	312/1201	0.85 (0.72–1.00)	400/1515	0.88 (0.77–1.00)	
p trend		0.03		0.03	0.90
	Family history: No		Family history: Yes		
No	2710/10859	1.00	502/1161	1.00	
Yes	1015/4521	0.86 (0.79–0.94)	189/418	1.04 (0.83–1.30)	0.18
<2 h/week	410/1946	0.91 (0.80–1.02)	66/186	0.88 (0.64–1.23)	
2+ h/week	591/2487	0.85 (0.76–0.94)	121/229	1.16 (0.88–1.53)	
p trend		0.002		0.44	0.09
	BMI <30 kg/m^2		BMI ≥30 kg/m^2		
No	1647/6317	1.00	1514/5586	1.00	
Yes	750/3265	0.87 (0.78–0.96)	434/1623	0.90 (0.79–1.03)	0.89
<2 h/week	294/1309	0.95 (0.82–1.10)	176/804	0.84 (0.69–1.00)	
2+ h/week	451/1903	0.83 (0.73–0.95)	248/782	0.96 (0.81–1.14)	
p trend		0.005		0.30	0.86
	Nulliparous		Parous		
No	498/2065	1.00	2699/9905	1.00	
Yes	235/1145	0.84 (0.69–1.01)	966/3782	0.89 (0.82–0.98)	0.71

Vigorous PA	Cases/Controls	OR (95 % CI)[a]	Cases/Controls	OR (95 % CI)[a]	*P* interaction
<2 h/week	80/462	0.76 (0.58–1.00)	393/1664	0.94 (0.83–1.06)	
2+ h/week	155/674	0.92 (0.73–1.16)	557/2036	0.87 (0.78–0.98)	
p trend		0.29		0.02	0.74

[a] All models were adjusted for age, study, time period, geographic region, education, age at menarche, parity, alcohol consumption, smoking, body mass index, first-degree family history of breast cancer, menopausal status and age at menopause, and female hormone use, except for the stratification variable

Table 4

Vigorous physical activity in the recent past and risk of ER-positive and ER-negative invasive breast cancer, stratified by age, menopausal status, family history of breast cancer, body mass index, and parity, in the AMBER consortium

	ER+ breast cancer				ER− breast cancer			
Vigorous PA	**Cases**	**OR (95 % CI)[a]**	**Cases**	**OR (95 % CI)[a]**	**Cases**	**OR (95 % CI)[a]**	**Cases**	**OR (95 % CI)[a]**
	Age <50 yrs		Age ≥50 yrs		Age <50 yrs		Age ≥50 yrs	
No	476	1.00	1358	1.00	340	1.00	617	1.00
Yes	199	0.79 (0.65–0.96)	449	0.90 (0.80–1.02)	196	0.98 (0.79–1.20)	221	0.91 (0.76–1.08)
Hours/week								
<2	70	0.85 (0.64–1.12)	209	0.97 (0.82–1.14)	56	0.95 (0.69–1.30)	86	0.87 (0.69–1.10)
2+	129	0.75 (0.60–0.94)	232	0.87 (0.74–1.03)	140	1.00 (0.79–1.26)	131	0.96 (0.77–1.19)
p trend		0.01		0.11		0.95		0.49
p interaction		0.28				0.32		
	Premenopause		Postmenopause		Premenopause		Postmenopause	
No	518	1.00	1210	1.00	347	1.00	536	1.00
Yes	207	0.79 (0.65–0.94)	409	0.95 (0.83–1.08)	176	0.91 (0.74–1.12)	202	0.95 (0.79–1.14)
Hours/week								
<2	78	0.79 (0.60–1.03)	191	1.05 (0.89–1.25)	51	0.78 (0.56–1.07)	79	0.96 (0.74–1.24)
2+	128	0.77 (0.62–0.96)	210	0.89 (0.75–1.06)	125	0.99 (0.78–1.26)	119	0.96 (0.76–1.20)
p trend		0.01		0.32		0.73		0.69
p interaction		0.12				0.63		
	Family history: No		Family history: Yes		Family history: No		Family history: Yes	
No	1544	1.00	290	1.00	812	1.00	145	1.00
Yes	541	0.86 (0.77–0.96)	107	1.04 (0.79–1.37)	355	0.91 (0.79–1.05)	61	1.12 (0.78–1.61)
Hours/week								
<2	240	0.96 (0.82–1.11)	39	0.91 (0.61–1.35)	119	0.86 (0.70–1.06)	23	1.04 (0.63–1.74)
2+	292	0.81 (0.70–0.93)	67	1.15 (0.82–1.61)	233	0.96 (0.81–1.14)	38	1.16 (0.75–1.81)
p trend		0.004		0.54		0.45		0.52
p interaction		0.07				0.70		
	Nulliparous		Parous		Nulliparous		Parous	
No	300	1.00	1527	1.00	129	1.00	823	1.00

	ER+ breast cancer				ER− breast cancer			
Vigorous PA	**Cases**	**OR (95 % CI)[a]**	**Cases**	**OR (95 % CI)[a]**	**Cases**	**OR (95 % CI)[a]**	**Cases**	**OR (95 % CI)[a]**
Yes	141	0.88 (0.69–1.12)	504	0.88 (0.78–0.99)	61	0.71 (0.50–1.01)	356	0.97 (0.84–1.12)
Hours/week								
<2	53	0.85 (0.61–1.18)	223	0.96 (0.82–1.13)	16	0.52 (0.30–0.90)	126	0.96 (0.78–1.18)
2+	88	0.94 (0.71–1.25)	271	0.83 (0.71–0.96)	45	0.86 (0.58–1.29)	226	0.98 (0.83–1.17)
p trend		0.54		0.02		0.25		0.79
p interaction		0.39				0.54		
	BMI < 30 kg/m^2		BMI ≥ 30 kg/m^2		BMI <30 kg/m^2		BMI ≥ 30 kg/m^2	
No	900	1.00	908	1.00	506	1.00	433	1.00
Yes	424	0.94 (0.82–1.07)	217	0.80 (0.67–0.94)	248	0.88 (0.74–1.04)	162	1.03 (0.83–1.27)
Hours/week								
<2	182	1.09 (0.91–1.30)	94	0.76 (0.60–0.96)	86	0.91 (0.71–1.16)	54	0.86 (0.63–1.17)
2+	238	0.86 (0.73–1.01)	117	0.83 (0.66–1.04)	161	0.88 (0.72–1.07)	105	1.16 (0.90–1.50)
p trend		0.14		0.02		0.18		0.45
p interaction		0.12				0.23		

[a]All models were adjusted for age, study, time period, geographic region, education, age at menarche, parity, alcohol consumption, smoking, body mass index, first-degree family history of breast cancer, menopausal status and age at menopause, and female hormone use, except for the stratification variable