Lifetime Physical Activity and Breast Cancer Risk in a Multiethnic Population: The San Francisco Bay Area Breast Cancer Study

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Abstract

Considerable epidemiological data have accumulated in support of a lower risk of breast cancer among physically active women. Few studies, however, have examined the relation with lifetime physical activity from all sources, and moderate activity in particular. We conducted a population-based case-control study of breast cancer in Latinas, African Americans, and whites aged 35–79 years to assess the association with lifetime histories of moderate and vigorous physical activity, including recreational activity, walking, bicycling, household and outdoor chores, and occupation. Patients diagnosed with invasive breast cancer between 1995 and 1998 were identified through the cancer registry in the San Francisco Bay area, and a random sample of women without breast cancer was identified through random-digit dialing. A structured questionnaire administered in-person was completed by 403 premenopausal cases and 483 controls and 847 postmenopausal cases and 1065 controls. Summing activities from all sources over an individual's lifetime, we found reduced breast cancer risk in both pre- and postmenopausal women with the highest *versus* lowest tertile of average lifetime activity (premenopausal: multivariate adjusted odds ratio = 0.74, 95% confidence interval = 0.52–1.05; postmenopausal: odds ratio = 0.81, 95% confidence interval = 0.64–1.02), with similar reductions in the three racial/ethnic groups. In premenopausal women, risk reductions were similar for different types of activities, whereas in postmenopausal women, they were limited to occupational activity. Considering the intensity of activities, risk reductions were similar for moderate and vigorous activities. Because few of the currently known risk factors for breast cancer are modifiable, these results underline the public health importance of promoting physically active lifestyles.

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Introduction

Since the first report in 1985 of a reduced risk of breast cancer among former college athletes (1), over 40 epidemiological studies have addressed this potentially modifiable lifestyle factor (2–7). As summarized by Friedenreich and Orenstein (7), 32 of 44 studies reported a decreased risk of breast cancer among women with the highest levels of physical activity, with risk reductions of up to 70%, average reductions ranging from 30% to 40%, and dose-response trends in some studies. Thus, considerable epidemiological data have accumulated supporting a lower risk of breast cancer among physically active women. The evidence, however, is not fully consistent, and several issues have not been adequately addressed. Most prior studies limited their exposure assessment to a single type of activity (*e.g.*, recreational activity or occupational activity) during a specific age period (*e.g.*, around the time of interview, in adolescence). Only one previous case-control study assessed lifetime activity from both occupational and nonoccupational sources (8). Incomplete assessment of total physical activity may have contributed to some of the inconsistent results. It remains uncertain whether a protective effect associated with physical activity differs between pre- and postmenopausal women or between different racial/ethnic groups that may have different activity patterns. Uncertainty also remains about the role of moderate activity in breast cancer prevention.

This population-based case-control study is one of the first to examine breast cancer risk in relation to lifetime histories of moderate and vigorous activities, including recreational activity, transportation (*i.e.*, walking and bicycling), household and outdoor chores, and occupation in a multiethnic population.

Materials and Methods

Study Population

Cases. We identified newly diagnosed breast cancer patients through the population-based cancer registry that covers the San Francisco Bay area and is part of the Surveillance, Epidemiology, and End Results (SEER) program and the California Cancer Registry. Eligible cases included Latina, African-American, and white women aged 35–79 years, diagnosed with a first primary invasive breast cancer between April 1, 1995 and April 30, 1998 and residing in the San Francisco Bay area (*i.e.*, San Francisco, San Mateo, Santa Clara, Alameda, and Contra Costa counties) at the time of diagnosis. Of 7591 identified cases, 297 (3.9%) were deceased, and 120 (1.6%) could not be contacted due to physician-reported contraindications. Of 7174 cases contacted by telephone, 6157 (86%) completed a screening interview that established study eligibility, assessed personal and family history of breast cancer, and verified race/ethnicity, which, as recorded in the cancer registry records, is not always consistent with self-report (9). Among nonparticipants, 487 (7%) were too ill or refused participation, 54 (1%) did not speak sufficient English or Spanish to complete the interview, 359 (5%) could not be located or had moved, and 117 (1%) could

not be reached despite more than 10 attempts over an extended period. Of 535 Latinas, 480 African Americans, and a 10% random sample of 524 whites, 1326 (86%) cases completed the in-person interview, including 468 (88%) Latinas, 409 (85%) African Americans, and 449 (86%) whites. Among the remaining cases, 149 declined participation, 42 were too ill, and 21 could not be located or reached after multiple attempts. One incomplete interview was excluded from the analysis.

Controls. We identified population controls through random-digit dialing. Using telephone numbers of recently diagnosed cancer patients and replacing the last two digits with random numbers, we generated 10 phone numbers per case number or a total of 74,673 numbers. Among the 45,378 numbers assessed as residential, nobody was reached (*i.e.*, no answer or answering machine only) at 10,012 numbers despite a minimum of 10 attempts over a 2–4-week period. Among the remaining 35,366 numbers, a household enumeration was completed for 28,775 (81%) numbers. From the pool of potentially eligible controls, 2389 were randomly selected according to the expected race/ethnicity and 5-year age distribution of cases, at approximate case:control ratios of 1:1 for African Americans and whites and 1:1.5 for Latinas. Thirteen control women were deceased by the time we attempted to contact them about the study. Among the remaining 2376 controls, 2062 (87%) were screened, 168 (7%) were too ill or refused to participate, 8 did not speak sufficient English or Spanish, and 138 (6%) had moved or could not be located. Of 806 Latina, 563 African-American, and 604 white controls invited to participate in the study, 1657 (84%) completed the in-person interview, including 697 (87%) Latinas, 461 (82%) African Americans, and 499 (83%) whites; 281 controls were too ill or declined participation, and 34 could not be located or reached after multiple attempts. One incomplete interview was excluded from the analysis.

Data Collection

Trained bilingual, bicultural interviewers administered a structured questionnaire on demographic and cultural background, residential history, physical activity, sunlight exposure, diet, supplement use, body size, change in weight, occupational history, menstrual and reproductive history, and medical history up to the reference year (defined as the year before diagnosis for cases or the year before selection into the study for controls). Usual dietary intake during the reference year was assessed using a food-frequency questionnaire adapted from Block's Health History and Habits Questionnaire (10, 11). In addition, the interviewers measured skin pigmentation, standing height, weight, and hip and waist circumferences.

The in-person interview included a comprehensive assessment of physical activity from multiple sources. Using a series of questions developed by Bernstein *et al.* (12) that assessed frequency, duration, and type of regular exercise throughout life, we included in our questionnaire a lifetime history of regular participation (at least 1 h/week for at least 4 months out of the year) in recreational activity, and we recorded the name of the activity, the ages when the activity started and ended, the number of hours/week and the number of months/year the study participant engaged in the activity. To aid recall, we presented cards to participants listing examples of vigorous and moderate recreational activities.

To assess daily living activities, we asked about regular (at least 20 min/day for at least 4 months out of the year) walking and bicycling to school and work and regular (at least 2 h/week for at least 4 months out of the year) strenuous household chores and strenuous outdoor chores. For each type of activity, we asked about the ages when the activity started and ended, and the number of hours/week and months/year the activity was performed. We limited the assessment to strenuous chores because recall is more reliable than for light activities (13). To aid recall, we presented cards with examples of strenuous activity appropriate for our multiethnic and migrant study population, including strenuous household chores such as scrubbing floors, sweeping, and washing windows and strenuous outdoor chores such as farm work, yard work, picking fruit, digging, mowing the lawn, and chopping wood. The lifetime histories of walking, bicycling, and strenuous chores recorded as many episodes of activity as the participant reported. Lastly, we assessed occupational physical activity through a lifetime occupational history. For each job held for at least 1 year, we recorded job title and type of business or industry, ages when job started and ended, number of hours worked/week, and self-assessed level of physical activity (*i.e.*, mostly sitting, mostly standing or walking, mostly moderate physical activities, mostly strenuous activities or hard labor).

Exposure Variables

For each source of physical activity (*i.e.*, recreation, transportation, chores, jobs) we estimated the average number of hours spent per week between age at menarche and the reference age by summing the hours of activity and dividing by the number of years between menarche and reference year. For occupational physical activity, we estimated the average number of hours worked per week in jobs that were assessed as mostly moderately active or mostly strenuous or hard labor. We estimated average lifetime total activity by summing the average weekly hours for each of the four sources of activity.

To consider the intensity of activity, we assigned a MET[1] value to each reported activity using the compendium by Ainsworth *et al.* (14). The MET value is the ratio of the metabolic rate for a specific activity compared with the resting metabolic rate. We multiplied the MET value for a specific activity by the number of hours/week spent in that activity to estimate MET-hours for each episode of activity, and we estimated average MET-hours of total activity by summing the MET-hours for each type of activity. For specific recreational activities, we assigned the MET scores listed in the compendium (14), and for other activities, we assigned MET scores of 3.5 for walking, 6.0 for bicycling, 6.0 for strenuous outdoor chores, 5.0 for strenuous household chores, 4.0 for moderately active jobs, and 6.0 for strenuous jobs. We also distinguished between total vigorous activities and total moderate activities. Vigorous activities included recreational activities $\geq$6 MET, bicycling to school or work, outdoor chores, and strenuous jobs. Moderate activities included recreational activities ranging from 3 to 5.9 MET, walking to school or work, household chores, and moderate jobs.

Statistical Analysis

We used *t* tests to assess differences in physical activity among Latina, African-American, and white controls. We used unconditional logistic regression modeling to calculate ORs and 95% CIs as an estimate of the relative risk associated with the various physical activity measures. Except for recreational activity, we categorized total and specific types of activity ac-

[1] The abbreviations used are: MET, metabolic equivalent of energy expenditure; CI, confidence interval; HRT, hormone replacement therapy; OR, odds ratio; BMI, body mass index; IGF, insulin-like growth factor.

cording to the tertile distribution among all controls. For recreational activity, we categorized average activity according to the tertile distribution among white controls, to facilitate comparison of our results with those by Bernstein *et al.* (12) and Carpenter *et al.* (15), who used the same method to assess lifetime histories of recreational activity. We evaluated known and suspected risk factors for breast cancer as potentially confounding variables, and we used multivariate logistic regression to adjust for age, race/ethnicity (Latinas, African Americans, whites), country of birth (United States-born, foreign-born), education (some high school or less, high school graduate, some college, college graduate), family history of breast cancer in first-degree relatives (yes, no), prior biopsy for benign breast disease (yes, no), age at menarche (<12 years, 12–13 years, ≥14 years), age at first full-term pregnancy (<20 years, 20–24 years, 25–29 years, ≥30 years), parity (nulliparous, 1–2, 3–4, ≥5), months of breast-feeding (0, <12, ≥12), BMI (tertiles of BMI among controls), and age at natural or surgical menopause (<45 years, 45–54 years, ≥55 years). BMI as a measure of adiposity was computed as weight (kg) divided by height (m) squared based on measured height and weight or self-reported height and weight for the 9% of cases and 8% of controls who declined the body measurements. We assessed dose-response trends across ordinal values of categorical variables and interactions by including cross-product terms in logistic models.

We performed separate analyses for pre- and postmenopausal women. Women were considered postmenopausal if their periods had stopped more than 1 year before diagnosis/selection and if they had never used HRT or had used HRT only after the cessation of menses. Also included in this group were women who began using HRT before the cessation of menses but had attained age 55 years or older at the time of diagnosis/selection, and women who reported a bilateral oophorectomy and/or a hysterectomy. We excluded 49 cases and 64 controls under age 55 years for whom menopausal status could not be determined because they began using HRT before the cessation of menses. The remaining women were considered premenopausal.

After excluding individuals with missing information on other risk factors or implausibly high physical activity, we based the multivariate analyses on 886 premenopausal women (403 cases and 483 controls) and 1912 postmenopausal women (847 cases and 1065 controls).

Results

The distribution of the study population by race/ethnicity and age is shown in Table 1. The large majority of African Americans and whites were born in the United States, whereas two-thirds of Latina controls were foreign-born (premenopausal, 68%; postmenopausal, 67%). About half of all controls did not attend college (premenopausal, 46%; postmenopausal, 55%). This proportion was highest among Latinas (premenopausal, 66%; postmenopausal, 80%), intermediate among African Americans (premenopausal, 38%; postmenopausal, 47%), and lowest among whites (premenopausal, 17%; postmenopausal, 31%).

Associations with established and suspected breast cancer risk factors are presented in Table 1. In both pre- and postmenopausal women, increased breast cancer risk was associated with higher education, a family history of breast cancer, and nulliparity. Late age at first full-term pregnancy and a prior biopsy for benign breast disease increased risk among premenopausal women only. Decreased risks were associated with foreign country of birth, late age at menarche, high parity, and ≥12 months of breast-feeding. High BMI decreased risk among premenopausal women and postmenopausal women with a history of HRT use. Among postmenopausal women without a history of HRT use, high BMI slightly increased risk. In both pre- and postmenopausal women, there was no association with oral contraceptive use and caloric intake. HRT use did not increase risk in postmenopausal women, but late age at natural or surgical menopause increased risk. These findings are consistent with other studies (16, 17).

The lifetime averages for total activity from all sources (*i.e.*, recreational activity, walking, bicycling, household and outdoor chores, and occupation) or specific types of activities differed by race/ethnicity (Table 2). The weekly average of total activity was highest among Latina controls, intermediate among African Americans, and lowest among whites. Latinas spent significantly more time with strenuous household chores than whites and less time with recreational activity than African Americans and whites. Postmenopausal Latina and African-American women spent more time with moderate or strenuous jobs compared with whites. In all three racial/ethnic groups, most activities were of moderate intensity (<6 MET), with the highest proportion reported by African-American controls (premenopausal, 81%; postmenopausal, 84%), followed by Latinas (premenopausal, 79%; postmenopausal, 81%) and whites (premenopausal, 71%; postmenopausal, 80%). For moderate activities, the lifetime average was 14.1 h/week for premenopausal women and 15.3 h/week for postmenopausal women. For vigorous activities, the lifetime averages were 4.1 and 3.4 h/week, respectively.

Premenopausal women in the highest *versus* lowest tertile of lifetime total activity had a significant 40% reduction in breast cancer risk (OR = 0.60, adjusted for age and race/ethnicity; Table 3). Adjustment for other risk factors yielded a slightly weaker risk reduction of borderline significance (OR = 0.74). Risk decreased with increasing physical activity, although the dose-response trend was not significant (P_{trend} = 0.09). For postmenopausal women, the findings for total activity were similar. The highest tertile of total activity was associated with a significant OR of 0.76 (adjusted for age and race/ethnicity), which was reduced to 0.81 after multivariate adjustment. When we stratified the analysis by age, we found significantly reduced risks among the most physically active women both under age 50 years (multivariate adjusted OR = 0.69, CI = 0.49–0.98), as well as those aged 50 years and older (multivariate adjusted OR = 0.79, CI = 0.62–0.99).

Among both pre- and postmenopausal women, recreational activity was not associated with reduced risk (Table 3). Activities of daily living (*i.e.*, walking and bicycling as means of transportation and strenuous household and outdoor chores) were associated with significantly reduced risk (OR = 0.54, adjusted for age and race/ethnicity) among premenopausal women with the highest activity level (Table 3). Adjustment for other risk factors, however, attenuated the association (OR = 0.74) and rendered it nonsignificant. Among postmenopausal women, no risk reduction remained after multivariate adjustment. For total nonoccupational activity (*i.e.*, recreational activity, transportation, household and outdoor chores), ORs for pre- and postmenopausal women were 0.79 (CI = 0.54–1.13) and 0.98 (CI = 0.77–1.24), respectively.

Occupational physical activity was associated with reduced breast cancer risk among both pre- and postmenopausal women (Table 3). For women with the highest lifetime average of time spent in moderate or strenuous jobs compared with women who held only low activity jobs (*i.e.*, mostly sitting, standing or walking), ORs were 0.76 and 0.70, respectively.

Table 1 Breast cancer risk factors by menopausal status

	Premenopausal women			Postmenopausal women		
	Cases $n = 409$	Controls $n = 493$	OR[a] (95% CI)	Cases $n = 868$	Control $n = 1100$	OR[a] (95% CI)
Age in reference year (yrs)						
35–49	350	430		55	91	
50–64	59	63		445	549	
65–79	0	0		368	460	
Race/ethnicity						
Latina	169	234		284	442	
African American	127	130		276	321	
White	113	129		308	337	
Country of birth						
United States-born	307	317	1.0	699	765	1.0
Foreign-born	102	176	0.59 0.41–0.84	169	335	0.56 0.43–0.72
Education						
Some high school or less	52	129	1.0	228	371	1.0
High school graduate	73	98	1.85 1.17–2.93	185	236	1.20 0.92–1.57
Some college	147	139	2.64 1.73–4.03	273	296	1.39 1.08–1.80
College graduate	137	127	2.82 1.82–4.38	179	196	1.37 1.02–1.84
Family history of breast cancer in first-degree relatives						
No	349	447	1.0	722	961	1.0
Yes	57	46	1.53 1.01–2.33	145	139	1.33 1.03–1.71
Prior biopsy for benign breast disease						
No	343	460	1.0	674	882	1.0
Yes	65	33	2.60 1.67–4.05	189	215	1.10 0.89–1.38
Age at menarche (yrs)						
8–11	105	99	1.0	212	227	1.0
12–13	205	271	0.71 0.51–0.98	435	525	0.85 0.68–1.07
≥14	98	122	0.77 0.52–1.12	208	339	0.64 0.50–0.83
Age at menopause[b] (yrs)						
<44				314	432	1.0
45–54				402	533	1.03 0.84–1.25
≥55				105	87	1.61 1.15–2.23
Parity						
Nulliparous	85	66	1.17 0.75–1.84	126	107	1.37 0.95–1.97
1	87	74	1.0	108	128	1.0
2	125	149	0.74 0.50–1.09	212	233	1.08 0.79–1.49
3	63	88	0.64 0.40–1.00	165	235	0.84 0.61–1.17
4	22	65	0.29 0.16–0.52	120	140	1.04 0.73–1.48
≥5	27	51	0.47 0.29–0.77	137	257	0.66 0.47–0.92
Age at first full-term pregnancy (yrs)						
<20	66	118	1.0	214	284	1.0
20–24	111	148	1.42 0.98–2.07	297	383	1.04 0.83–1.32
25–29	80	79	1.91 1.26–2.91	150	204	0.98 0.74–1.30
≥30	67	81	1.74 1.12–2.69	80	110	0.98 0.70–1.38
Nulliparous	85	66	2.33 1.52–3.59	126	107	1.52 1.10–2.08
Lifetime breastfeeding (months)						
Nulliparous	85	66	1.36 0.91–2.01	126	107	1.28 0.95–1.72
0	113	120	1.0	362	405	1.0
<12	124	143	1.02 0.73–1.43	204	266	0.87 0.69–1.09
≥12	87	164	0.63 0.44–0.90	176	322	0.63 0.50–0.80
Use of oral contraceptives						
Never	53	91	1.0	386	528	1.0
Ever	315	399	1.35 0.93–1.97	379	552	0.93 0.75–1.15
Use of HRT						
Never				350	433	1.0
Ever				507	651	0.91 0.75–1.11
Caloric intake (tertiles)[c]						
Low	163	177	1.0	267	358	1.0
Medium	137	177	0.86 0.63–1.17	288	359	1.12 0.90–1.41
High	146	179	0.93 0.68–1.28	271	360	1.13 0.90–1.43
BMI (tertiles)						
<26.1	162	164	1.0			
26.1–31.9	126	162	0.76 0.55–1.06			
≥32.0	121	164	0.70 0.50–0.97			
BMI without history of HRT use						
<26.1				89	130	1.0
26.1–31.9				120	136	1.29 0.89–1.87
≥32.0				139	162	1.23 0.86–1.77
BMI with history of HRT use						
<26.1				215	230	1.0
26.1–31.9				154	219	0.79 0.60–1.05
≥32.0				137	199	0.80 0.60–1.07

[a] Adjusted for age and race/ethnicity.
[b] Natural or surgical menopause.
[c] Premenopausal women, <1789 Kcal/day, 1789–2584 Kcal/day, ≥2585 Kcal/day; postmenopausal women, <1530 Kcal/day, 1530–2190 Kcal/day, ≥2191 Kcal/day.

Table 2 Sources of average lifetime physical activity among control women, by race/ethnicity and menopausal status

Hours/week	Premenopausal controls			Postmenopausal controls		
	Latinas $n = 228$	African-Americans $n = 128$	Whites $n = 127$	Latinas $n = 421$	African-Americans $n = 316$	Whites $n = 328$
Total activity	19.9[a]	16.9	16.4	21.7[a,b]	18.1[a]	15.6
Recreational activity	1.9[a,b]	3.3	3.5	1.7[a,b]	2.3	2.7
Walking and bicycling	0.8[a,b]	0.6	0.5	0.7[a]	0.6[a]	0.4
Strenuous household chores	8.8[a,b]	6.3	5.9	10.5[a,b]	6.5	6.9
Strenuous outdoor chores	2.0[b]	0.5[a]	1.4	1.9[b]	1.0	1.4
Mostly moderate or strenuous jobs	6.3	6.2	5.1	6.9[a]	7.8[a]	4.3
Total vigorous activity	4.2	3.3	4.8	4.0	2.9	3.0
Total moderate activity	15.7[a]	13.6	11.6	17.6[a,b]	15.2[a]	12.6

[a] Statistically significant difference compared with whites ($P < 0.05$).
[b] Statistically significant difference compared with African-Americans ($P < 0.05$).

Consideration of intensity using MET-hours did not strengthen the results for total activity (Table 4). When we distinguished between moderate (<6 MET) and vigorous (≥6 MET) activities, we found similar risk reductions for the two types of activities.

Stratified analyses by race/ethnicity produced generally

Table 3 Lifetime[a] physical activity and breast cancer risk, by type of activity and menopausal status

Premenopausal women					Postmenopausal women				
Hours/week	Cases $n = 403$	Controls $n = 483$	OR[b] (95% CI)	OR[c] (95% CI)	Hours/week	Cases $n = 847$	Controls $n = 1065$	OR[b] (95% CI)	OR[d] (95% CI)
Total activity[e]					Total activity[e]				
<9.1	170	161	1.0	1.0	<9.6	335	354	1.0	1.0
9.1–20.7	133	160	0.79 0.58–1.09	0.88 0.63–1.22	9.6–21.6	267	355	0.80 0.64–1.00	0.84 0.67–1.06
≥20.8	100	162	0.60 0.43–0.83	0.74 0.52–1.05	≥21.7	245	356	0.76 0.61–0.95	0.81 0.64–1.02
Recreational activity					Recreational activity				
<1.5	200	250	1.0	1.0	<0.7	339	474	1.0	1.0
1.5–3.9	97	118	1.00 0.72–1.40	0.91 0.64–1.29	0.7–2.6	258	302	1.17 0.94–1.46	1.08 0.86–1.36
≥4.0	106	115	1.12 0.80–1.55	1.02 0.72–1.46	≥2.7	250	289	1.17 0.94–1.46	1.14 0.90–1.44
Total daily living activity[f]					Total daily living activity[f]				
<4.0	164	161	1.0	1.0	<4.3	315	354	1.0	1.0
4.0–9.6	153	160	0.94 0.69–1.29	1.04 0.75–1.45	4.0–9.6	274	355	0.86 0.69–1.07	0.89 0.71–1.12
≥9.7	86	162	0.54 0.38–0.76	0.74 0.50–1.08	≥9.7	258	356	0.86 0.68–1.07	0.98 0.77–1.25
Walking and bicycling					Walking and bicycling				
<0.2	158	160	1.0	1.0	<0.14	275	355	1.0	1.0
0.2–0.5	134	162	0.84 0.61–1.15	0.75 0.53–1.05	0.14–0.42	288	353	1.03 0.82–1.29	0.98 0.78–1.23
≥0.6	111	161	0.72 0.52–1.01	0.73 0.51–1.03	≥0.43	284	357	1.04 0.83–1.30	1.03 0.81–1.30
Strenuous household chores					Strenuous household chores				
<3.3	167	161	1.0	1.0	<3.4	322	355	1.0	1.0
3.3–7.3	137	160	0.81 0.59–1.12	0.88 0.62–1.24	3.4–7.8	261	354	0.79 0.64–0.99	0.88 0.70–1.12
≥7.4	99	162	0.60 0.43–0.84	0.81 0.53–1.24	≥7.9	264	356	0.86 0.69–1.07	1.20 0.90–1.61
Strenuous outdoor chores					Strenuous outdoor chores				
0	237	240	1.0	1.0	0	391	479	1.0	1.0
0.1–1.1	91	122	0.75 0.54–1.05	0.82 0.58–1.15	0.1–0.9	236	293	0.96 0.77–1.19	0.97 0.77–1.21
≥1.2	75	121	0.64 0.46–0.91	0.81 0.56–1.18	≥1.0	220	293	0.92 0.73–1.14	1.01 0.80–1.27
Mostly moderate or strenuous jobs					Mostly moderate or strenuous jobs				
0	237	250	1.0	1.0	0	471	513	1.0	1.0
0.1–10.2	90	117	0.83 0.60–1.16	0.90 0.64–1.28	0.1–9.0	200	276	0.79 0.63–0.98	0.81 0.65–1.02
≥10.3	76	116	0.69 0.49–0.97	0.76 0.53–1.10	≥9.1	176	276	0.71 0.56–0.89	0.70 0.55–0.88

[a] From menarche to reference year.
[b] Adjusted for age and race/ethnicity.
[c] Adjusted for age, race/ethnicity, country of birth, education, family history of breast cancer, prior biopsy for benign breast disease, age at menarche, parity, age at first full-term pregnancy, breast-feeding, BMI, and other components of total activity.
[d] Adjusted for age, race/ethnicity, country of birth, education, family history of breast cancer, age at menarche, parity, breast-feeding, age at menopause, and other components of total activity.
[e] Includes recreational activity, walking, bicycling, strenuous household and outdoor chores, and non-sedentary jobs.
[f] Includes walking, bicycling, and strenuous household and outdoor chores.

Table 4 Lifetime[a] physical activity[b] and breast cancer risk, by intensity of activity

Premenopausal women							Postmenopausal women					
Hours/week	Cases $n = 403$	Controls $n = 483$	OR[c] (95% CI)		OR[d] (95% CI)		Hours/week	Cases $n = 847$	Controls $n = 1065$	OR[c] (95% CI)		OR[e] (95% CI)	
Total activity (MET-hours per week)							Total activity (MET-hours per week)						
<45	171	161	1.0		1.0		<45	332	354	1.0		1.0	
45–99	124	160	0.74	0.54–1.02	0.81	0.58–1.14	45–102	268	355	0.81	0.65–1.01	0.85	0.68–1.07
≥100	108	162	0.64	0.46–0.89	0.78	0.55–1.10	≥103	241	356	0.77	0.62–0.96	0.82	0.65–1.03
Total moderate[f] activity							Total moderate[f] activity						
<6.8	162	161	1.0		1.0[g]		<7.6	343	354	1.0		1.0[g]	
6.9–16.6	151	160	0.94	0.69–1.29	1.05	0.75–1.47	7.6–17.7	271	356	0.79	0.64–0.98	0.85	0.68–1.06
≥16.7	90	162	0.56	0.40–0.78	0.67	0.46–0.96	≥17.8	233	355	0.70	0.56–0.88	0.74	0.59–0.94
Total vigorous[h] activity							Total vigorous[h] activity						
<6.8	343	403	1.0		1.0[i]		<7.6	758	940	1.0		1.0[i]	
6.9–16.6	47	49	1.13	0.74–1.73	1.07	0.68–1.68	7.6–17.7	65	72	1.02	0.72–1.43	1.13	0.79–1.60
≥16.7	13	31	0.50	0.26–0.97	0.68	0.34–1.37	≥17.8	24	43	0.72	0.43–1.21	0.87	0.51–1.48

[a] From menarche to reference year.
[b] Includes recreational activity, walking, bicycling, strenuous household and outdoor chores, and nonsedentary jobs.
[c] Adjusted for age and race/ethnicity.
[d] Adjusted for age, race/ethnicity, country of birth, education, family history of breast cancer, prior biopsy for benign breast disease, age at menarche, parity, age at first full-term pregnancy, breast-feeding, and BMI.
[e] Adjusted for age, race/ethnicity, country of birth, education, family history of breast cancer, age at menarche, parity, breast-feeding, and age at menopause.
[f] Moderate activities 3–5.9 METS.
[g] Adjusted for above variables and total vigorous activity.
[h] Vigorous activities ≥6 METS.
[i] Adjusted for above variables and total moderate activity.

similar results for Latinas, African Americans, and whites (Table 5). However, given the relatively small sample sizes, none of the risk reductions were statistically significant. For total activity from all sources, ORs for the highest tertile of activity ranged from 0.68 to 0.76 among premenopausal women and from 0.71 to 0.91 among postmenopausal women. For specific types of activity, ORs were generally similar, except for exercise that reduced premenopausal breast cancer risk among Latinas and whites only. We assessed modifying effects of age, parity, BMI, and family history of breast cancer on the association with physical activity, but none of the interactions was statistically significant.

Discussion

Among the many studies that examined breast cancer risk in relation to physical activity, our study is only the second to assess lifetime physical activity in terms of frequency, duration, and intensity of all types of moderate and vigorous activities, including recreational activity, transportation, household and outdoor chores, and occupational activities. We found reduced risks of breast cancer of borderline statistical significance among the most physically active premenopausal (OR = 0.74) and postmenopausal (OR = 0.81) women. When we stratified the study population by age instead of menopausal status, risks were significantly reduced among women under age 50 years (OR = 0.69) and those aged 50 years and older (OR = 0.79). Thus, our study adds to the epidemiological evidence that supports a modest reduction in both pre- and postmenopausal breast cancer risk among physically active women.

Our findings for premenopausal women are in agreement with previous reports from cohort studies (18–22), population-based case-control studies (12, 23–32), and clinic-based case-control studies (33–38), although several studies found no association with breast cancer risk in premenopausal or younger women (8, 39–44). Several studies, including ours, found a risk reduction in postmenopausal women, with supporting evidence from cohort studies (19, 25, 39, 42, 45–48), population-based case-control studies (8, 15, 23, 29–31, 49, 50), and clinic-based case-control studies (34, 35, 37, 38). Several studies found no risk reduction in postmenopausal or older women (18, 21, 22, 343, 51, 52) or women of all ages combined (53–55). We found similar risk reductions in pre- and postmenopausal women, which is consistent with other studies that assessed risk in both groups (19, 23, 24, 27, 30, 34, 35, 37, 38, 56). Some studies found a reduced risk in premenopausal or younger women only (18, 21, 22, 33), whereas others found a lower risk in postmenopausal women only (8, 39, 42, 47) or stronger protective effects in postmenopausal women compared with premenopausal women (25, 31). Although not fully consistent, considerable epidemiological evidence has accumulated that physical activity reduces breast cancer risk in both pre- and postmenopausal women.

Unlike most other studies, we examined the relation between physical activity and breast cancer risk in a multiethnic population. To date, only two United States studies assessed the association with physical activity in Latinas (29) and African Americans (30). In a case-control study by Gilliland *et al.* (29), high levels of total nonoccupational activity (*i.e.*, exercise, housework, and heavy outside work) around the time of diagnosis were associated with a greatly reduced risk among Hispanic women (OR = 0.29), but not among whites. In a nested case-control study of African-American women, risk associated with strenuous recreational activity at ages 21 and 30 years was reduced by 50% (30). Our findings suggest that the risk reductions are similar among Latinas, African Americans, and whites, despite different activity patterns in the three populations.

The risk reductions found in this study are within the range

Table 5 Lifetime[a] physical activity and breast cancer risk, by race/ethnicity and menopausal status

Hours/week	Premenopausal women			Hours/week	Postmenopausal women		
	Latinas 166 cases 228 controls	African-Americans 124 cases 128 controls	Whites 113 cases 127 controls		Latinas 278 cases 421 controls	African-Americans 270 cases 316 controls	Whites 299 cases 328 controls
	OR[b] (95% CI)	OR[b] (95% CI)	OR[b] (95% CI)		OR[c] (95% CI)	OR[c] (95% CI)	OR[c] (95% CI)
Total activity				Total activity			
<9.1	1.0	1.0	1.0	<9.6	1.0	1.0	1.0
9.1–20.7	0.84 0.49–1.45	1.00 0.55–1.84	0.82 0.42–1.58	9.6–21.6	0.82 0.55–1.24	0.78 0.52–1.17	0.94 0.64–1.37
≥20.8	0.73 0.42–1.28	0.68 0.35–1.34	0.76 0.36–1.61	≥21.7	0.81 0.54–1.22	0.71 0.47–1.07	0.91 0.60–1.41
Total moderate activity[d]				Total moderate activity[d]			
<6.8	1.0	1.0	1.0	<7.6	1.0	1.0	1.0
6.9–16.6	1.01 0.58–1.76	1.32 0.69–2.50	1.06 0.54–2.07	7.6–17.7	0.74 0.49–1.13	0.85 0.57–1.27	1.03 0.70–1.52
≥16.7	0.82 0.47–1.46	0.77 0.38–1.56	0.44 0.20–0.99	≥17.8	0.71 0.47–1.05	0.60 0.40–0.92	1.02 0.66–1.59
Recreational activity				Recreational activity			
<1.5	1.0	1.0	1.0	<0.7	1.0	1.0	1.0
1.5–3.9	0.77 0.43–1.38	1.20 0.61–2.39	0.81 0.41–1.60	0.7–2.6	1.28 0.86–1.89	0.99 0.65–1.51	1.07 0.72–1.60
≥4.0	0.76 0.41–1.42	1.37 0.73–2.55	0.79 0.39–1.60	≥2.7	1.38 0.90–2.10	1.04 0.69–1.57	1.13 0.76–1.70
Total daily living activity[e]				Total daily living activity[e]			
<4.0	1.0	1.0	1.0	<4.3	1.0	1.0	1.0
4.0–9.4	1.11 0.63–1.93	1.02 0.57–1.83	0.91 0.46–1.77	4.0–10.4	1.14 0.74–1.76	0.76 0.52–1.12	0.81 0.55–1.20
≥9.5	0.65 0.36–1.16	0.81 0.38–1.73	0.71 0.30–1.67	≥10.5	1.00 0.66–1.50	0.91 0.58–1.44	1.10 0.71–1.71
Mostly moderate or strenuous jobs				Mostly moderate or strenuous jobs			
0	1.0	1.0	1.0	0	1.0	1.0	1.0
0.1–9.9	1.07 0.62–1.84	0.88 0.43–1.81	0.93 0.46–1.85	0.1–9.0	0.88 0.59–1.32	1.01 0.66–1.52	0.65 0.44–0.96
≥10.0	0.87 0.49–1.55	0.67 0.35–1.28	0.87 0.40–1.91	≥9.1	0.68 0.46–1.01	0.77 0.51–1.16	0.62 0.39–1.00

[a] From menarche to reference year.
[b] Adjusted for age, country of birth, education, family history of breast cancer, prior biopsy for benign breast disease, age at menarche, parity, age at first full-term pregnancy, breast-feeding, and BMI.
[c] Adjusted for age, country of birth, education, family history of breast cancer, age at menarche, parity, breast-feeding, and age at menopause.
[d] Adjusted for above variables and total vigorous activity.
[e] Includes walking, bicycling, and strenuous household and outdoor chores.

(20–40%) of what other investigators have reported (5). It is difficult, however, to directly compare the magnitude of risk reductions across studies and derive a quantitative estimate of risk reduction associated with a specific level of physical activity. Previous studies have used many different approaches to measure physical activity, ranging from single questions about usual activity to detailed lifetime histories. Some studies assessed only a single type of activity (*e.g.*, recreational activity) or considered only a single age period (*e.g.*, adolescence). The findings from such studies are difficult to interpret. Individuals with little recreational activity may have energy expenditure from other activities and are therefore not necessarily sedentary. In our study, Latina women had the lowest lifetime average of time spent in recreational activity, yet they had the highest lifetime average when considering activities from all sources, including household and outdoor chores. Similarly, activity during a specific age period may not represent lifetime activity because physical activity often changes with age (57). Furthermore, it has not been established what age periods are etiologically most relevant. Four studies (8, 12, 15, 28) emphasize the importance of assessing lifetime physical activity. Incomplete assessment of total activity is likely to result in exposure misclassification and may have contributed to some of the inconsistent results, possibly attenuating relative risk estimates.

We addressed the methodologic limitations of previous studies by assessing detailed lifetime histories of all types of physical activities that included the ascertainment of type, frequency, duration, and intensity of activities. The assessment of all types of activities is particularly important in studies of women and ethnically diverse populations. As others have reported (58–60), we found that household and outdoor chores are important contributors to total activity and that activity patterns differ considerably between racial/ethnic groups. It has also been shown that the reporting of activities varies between racial/ethnic groups, with African Americans being less likely to report activities of daily living as physical activity compared with whites (61). These observations underline the importance of inquiring about specific types of activities (*i.e.*, recreational activity, transportation, household and outdoor chores, occupation) to fully assess total physical activity in a multiethnic population.

Our comprehensive lifetime assessment of physical activity is most comparable with the lifetime assessment developed by Friedenreich *et al.* (13), which focused on lifetime histories of light, moderate, and vigorous activities from all sources and was applied in a recent population-based case-control study of breast cancer (8). In contrast to our findings, that study in mostly white women living in Alberta, Canada found no association between lifetime total activity and premenopausal breast cancer risk. The reasons for these discrepant findings are not obvious. For postmenopausal women, both our and Friedenreich's study found a lower risk among women with the highest level of total activity (OR = 0.81 and OR = 0.70, respectively). Both our and Friedenreich's study assessed lifetime exercise histories using the approach developed by Bernstein *et al.* (12) for a study of white women under age 40 years living in Los Angeles. Friedenreich *et al.* (8) found no association with

exercise among premenopausal women, we found an OR of 0.79 among white women with a lifetime average of 4 or more hours of exercise/week, whereas Bernstein *et al.* (12) reported an OR of 0.42 (CI = 0.27–0.64) for women with a lifetime weekly average of 3.8 or more hours of exercise. Our population of white women under age 40 years was too small for separate analysis.

Several potential limitations need to be considered. Nonresponse raises concern about potential selection bias. At the screening and interview level, our response rates were similar for cases and controls, and they differed little by race/ethnicity. For the identification of controls, we relied on random-digit dialing, a method that is becoming more difficult to use, given the relatively high percentage of residential numbers where nobody could be reached, despite multiple attempts. Thus, the overall response rate was lower among controls than among cases. It is reassuring, however, that our associations with standard risk factors are consistent with other studies (16, 17).

In case-control studies the assessment of lifetime histories of physical activity relies on recall over long periods of time. Given the better recall of moderate and vigorous activities compared with light activities (13, 62, 63), we focused the assessment on moderate and vigorous activities (≥3.0 MET). Although the lifetime history of recreational activity allowed the recording of light activities (<3.0 MET), the vast majority of reported recreational activities were of moderate intensity. Three prior studies assessed the reliability of self-reported lifetime physical activity and found generally high reproducibility (12, 63–65). When we initiated this study in 1995, few studies had been published on the association between physical activity and breast cancer risk, thus minimizing public awareness of this potentially protective lifestyle factor. Nevertheless, the possibility of exposure misclassification cannot be ruled out.

Unlike some other studies, we assessed confounding by a broad range of factors. Although most previous studies found no evidence of confounding (3), adjustment for other risk factors did attenuate the risk reductions in our study, particularly among premenopausal women. For total physical activity, the significant OR of 0.60 (adjusted for age and race/ethnicity) changed to 0.67 after adjustment for education and parity and to 0.74 after adjustment for additional risk factors included in the final model. These findings underline the importance of adequate control for confounding.

It has not been established whether the association with physical activity is modified by other risk factors. Stratified analyses by parity (8, 12, 20, 24, 25, 28, 35), BMI (8, 12, 19, 25, 26, 28, 32, 35, 41–43 49, 50), and family history (8, 28, 41, 43) have produced inconsistent results. We did not find any statistically significant modifying effects, but larger studies are needed to identify subgroups that may benefit to a greater extent from an active lifestyle.

Studies in young athletes and dancers have long documented a higher frequency of menstrual and hormonal disturbances, including delayed onset of menstruation, secondary amenorrhea, anovulatory and irregular cycles, shortened luteal phase, and lower estrogen levels (66–69). Lower estrogen levels, anovulatory cycles, and luteal phase deficiencies have also been reported in women athletes (70–72). These menstrual and hormonal characteristics in turn have been associated with breast cancer risk (73, 74), thereby supporting the plausibility that physical activity may lower breast cancer risk through its influence on ovarian function. Physical activity may also reduce breast cancer risk by preventing weight gain or reducing body fat, which is the primary source of estrogen production in postmenopausal women (75). In addition, the influence of physical activity on breast cancer risk may be mediated through effects on other hormones, such as IGFs (76, 77). Data on the effect of physical activity on IGF and IGF-binding proteins, however, are limited and remain inconclusive (78).

From the current epidemiological literature, it is not clear whether a beneficial influence on breast cancer risk is limited to vigorous activities or whether moderate-intensity activities also play a role in lowering risk. There is some evidence suggesting that menstrual and hormonal effects may not be limited to intensive or competitive athletic training. Moderate recreational activities have been linked to delays in menarche, and shorter and anovulatory cycles in young girls (79, 80), as well as irregular and longer cycles (81–83), anovulatory cycles (84), luteal phase deficiencies (84), and lower levels of estrogen and progesterone (85, 86) in premenopausal women. Moderate physical activity has also been associated with lower estrogen and progesterone levels in postmenopausal women (87, 88), although the data are not consistent (89). Thus, it appears that physical activity is associated with various menstrual and hormonal disturbances which, depending on the intensity, range from obvious menstrual alterations such as late menarche and secondary amenorrhea to more subtle hormonal effects that may occur when menstrual cycles seem normal, including anovulatory cycles and lower estrogen levels.

When we distinguished between moderate and vigorous activities from all sources, we found similar risk reductions for the two types of activities. The examination of MET-hours/week *versus* hours/week also produced similar results. In three other studies (28, 55, 90), vigorous activities did not further reduce risk compared with moderate activities. These findings suggest that duration of activity may be more important in breast cancer risk reduction than intensity of activity and that moderate-intensity activities are sufficient to decrease risk. Given that more women engage in moderate-intensity activities than vigorous activities, these findings are of major public health importance.

In conclusion, this study supports previous reports of a reduced risk of breast cancer in physically active women. Considering all types of physical activity, we noted modest risk reductions in women with the highest level of lifetime physical activity that were similar in pre- and postmenopausal women, and in the three racial/ethnic groups. Most importantly, we found similar risk reductions for moderate and vigorous activities. Because few breast cancer risk factors have been identified that are potentially modifiable, our data support the importance of physically active lifestyles in lowering the risk of developing breast cancer.

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