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Occupational physical activity and risk for breast cancer in a nationwide cohort study in Sweden

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Abstract

Objective: Our purpose was to investigate effects of physical activity on risk for breast cancer.
Methods: From the Swedish nationwide censuses in 1960 and 1970 we defined three partly overlapping cohorts of women whose occupational titles allowed reproducible classification of physical demands at work in 1960 (n = 704,904), in 1970 (n = 982,270), or with the same demands in both 1960 and 1970 (n = 253,336). The incidence of breast cancer during 1971–89 was ascertained through record linkage to the Swedish Cancer Register. We used Poisson regression to estimate relative risks (RR).
Results: A total of 20,419, 22,840, and 8261 breast cancers, respectively, were detected in the three cohorts. In all three cohorts the risk for breast cancer increased monotonically with decreasing level of occupational physical activity and with increasing socioeconomic status. Among women with the same estimated physical activity level in 1960 and 1970 the RR was 1.3 for sedentary as compared with high/very high activity level (95% CI 1.2–1.4; p for trend < 0.001). Adjustment for socioeconomic status virtually eliminated this association (RR 1.1; 95% CI 0.9–1.2; p for trend 0.12) leaving a statistically significant 30% gradient only among women aged 50–59 years at follow-up. The association between socioeconomic status and breast cancer risk was largely unchanged after adjustment for occupational physical activity.
Conclusion: The protective effect of occupational physical activity on breast cancer risk, if any, appears to be confined to certain age groups.

Introduction

The hypothesis that physical activity reduces a woman's risk for breast cancer has received increasing attention recently [1–27]. The theory is biologically plausible because high energy expenditure, for example, may be associated with reduced sex hormone levels [28] and prevents obesity [29], established risk factors among postmenopausal women [30, 31]. Physical activity during reproductive years may reduce levels of circulating ovarian hormones and the frequency of regular cycles [32–35], thus reducing the cumulative exposure to ovarian hormones (estrogen and progesterone). If a true causal association exists, increased physical activity would be one of the few realistic targets for primary prevention of breast cancer in women.

The epidemiological evidence that high physical activity reduces breast cancer incidence is, however, far from conclusive. Although several studies are clearly supportive [1, 5, 12, 13, 15, 16, 18, 22, 24], no association was observed in other studies of cohort [6, 11, 26] or case–control [23, 25] design. Interpretation is often hampered by small sample size [11, 21], restriction to young women [9, 12, 25, 26], analyses of extreme levels of physical activity [1, 6, 16], or assessment of activity only at a single point in time [8, 14, 22]. In addition,

several investigators assessed only leisure-time activity [15, 18, 23, 25], while occupational activity is likely to account for a larger part of a woman's total energy expenditure during adulthood. The need for very large studies of occupational physical activity, with repeated exposure assessment, was emphasized recently [36].

We used the nationwide Swedish Cancer–Environment Register III to assess risk for breast cancer in relation to occupational physical activity. We focused on women with the same level of occupational physical activity at two assessments 10 years apart. The large number of observed breast cancer cases allowed detailed analyses stratified by age at entry and age at follow-up. We were also able to assess separately the risk in women who were estimated as having changed in the level of physical activity.

Subjects and methods

Census data

Census information has been obtained regularly in Sweden using questionnaires mailed to every household. The questionnaires cover demographic, occupational (including employment status, job title, industry and work address), and socioeconomic factors for each household member during one week in October [37]. The data are stored together with the national registration number – a unique personal identifier assigned to all Swedish residents [38] – which allows linkage between registers. Since participation is mandatory by law, the censuses are more than 99% complete [39, 40].

The Cancer and Cancer–Environment Register

The national Swedish Cancer Register, established in 1958, includes more than 98% of all diagnosed cancer cases in the country [41]. It contains demographic and tumor data (ICD-7 and histopathology codes, date of diagnosis, mode of diagnosis but no tumor stage). The Cancer Register is linked annually to the Swedish Register of Causes of Death, which provides information on the underlying and contributing causes of death derived from the obligatory death certificates [42].

The Cancer–Environment Register III (CERIII) was established by adding census data from 1960 and 1970 to the Cancer Register from 1971 to 1989 [43]. The CERIII proper, thus, includes cancer patients who resided in Sweden both in 1960 and 1970 (and thus are recorded in both censuses), and encompasses a total of 392,941 women with 440,819 tumors. As a supplement to the CERIII proper, there is a background register with *all* Swedish residents who took part in both the 1960 and 1970 censuses. Except for tumor data, the information in this background register is the same as in the CERIII proper, including dates (but not causes) of death among the deceased. The background register included 3,347,867 women in 1971. After record linkages, the national registration numbers were removed from both the CERIII proper and the background register to ensure confidentiality.

Classification of occupational physical activity and covariates

The occupations reported in the census questionnaires were coded into 245 categories in the 1960 census and 248 categories in the 1970 census [44]. This coding scheme, devised by the National Labor Market Board in Sweden [37] in collaboration with the National Labor Market Government in Denmark, Norway, and Finland [45], parallels the classification of the International Labor Office and the United Nations [46].

We classified each occupation as demanding very high, high, moderate, light, or sedentary physical activity. Assessments were done independently by three Swedish specialists in occupational medicine with extensive experience in job classification. To reduce misclassification, we considered in the present analysis only occupations consistently classified by the three experts; we required absolute agreement between at least two of the experts while the third was allowed to diverge by no more than one category. A total of 202 occupations were thus unequivocally classified. Because few women were classified as having jobs with very high demands, the two categories of highest physical activity were subsequently merged. The physical activity categories have been described previously [47]. A validation study in a historic cohort of twins showed strong agreement between the experts' scoring and self-reports of job-related physical activity given in the 1960s [47].

Socioeconomic status was categorized into four levels (unskilled blue-collar, skilled blue-collar, less educated white-collar, educated white-collar occupations), based on the occupational title, as described in detail elsewhere [48]. We categorized the place of residence into two categories: cities with a population exceeding 200,000 (Stockholm, Gothenburg, and Malmö) *versus* the rest of Sweden.

Study cohorts

A total of 704,904 women in the background register reported employment in the 1960 census (but not necessarily also in the 1970 census) in a job that we

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could unequivocally classify with regard to physical activity. There were 982,270 women with such jobs reported in the 1970 census (but not necessarily also in the 1960 census). We further identified the 253,336 women who had jobs classified as demanding the *same* physical activity level both in 1960 and 1970 censuses.

Follow-up

To ascertain cancer incidence and dates of diagnosis in these cohorts, we linked the background register to the CERIII proper, matching on all available census variables in both data sets. We only analyzed first invasive cancers. Person-years were calculated from 1 January 1971 until the diagnosis of any malignant tumor, death, or end of follow-up (31 December 1989), whichever occurred first. Cancers diagnosed incidentally first at autopsy were not counted.

Analyses

We analyzed data in a grouped form. Attained age (age at follow-up) was divided into eleven 5-year categories (< 40, 40–44,..., 80–84, 85+ years). The 19 calendar years of follow-up were divided into nine 2-year intervals and one 1-year (1 January 1971–31 December 1972, 1973–74,..., 1 January 1989–31 December 1989).

First we made external comparisons with the entire Swedish population. The expected number of breast cancers was calculated by multiplying the number of person-years observed in 5-year age and calendar year strata in the cohorts by the stratum-specific breast cancer incidence rates, derived from the Swedish Cancer Register. The relative risk (RR) was estimated by the standardized incidence ratio (SIR), defined as the ratio of observed number of cancers to those expected. The 95% confidence interval was calculated on the assumption that the observed numbers of cancers follow a Poisson distribution.

We then made internal comparisons between exposure groups within the cohort with adjustment for available co-variates using Poisson models estimated by the maximum likelihood method (EPICURE/AMFIT) [49], and with rate ratios as the measure of relative risk. Estimated occupational physical activity level, attained age (age at follow-up), calendar year of follow-up, and place of residence, were the explanatory variables in the baseline model. Socioeconomic status was adjusted for in expanded multivariate models. The deviance was of the same order as the degrees of freedom. Thus no correction for overdispersion was necessary [50].

Results

During the 19 years of follow-up we observed 20,419, 22,840, and 8261 cases of primary invasive breast cancer in the three cohorts of women who had classifiable jobs in 1960, 1970, and in both 1960 and 1970 censuses, respectively. The distribution of person-years by category of estimated occupational physical activity, the number of observed cases, and SIRs with 95% CI are shown in Table 1. Women with moderate to high occupational physical activity had a breast cancer incidence that was close to the expected in the Swedish female population, whereas women with light or sedentary jobs had increased risks.

Table 1. Characteristics of the cohort, by occupational physical activity level in 1960 and 1970, number of women at risk at start of follow-up in 1971, number of person-years at risk, number of incident cases of primary breast cancer during follow-up through 1989 (No.), standardized incidence ratio (SIR) and 95% confidence interval (CI)

Census	Occupational physical activity	Number of women at risk	Number of person-years	Number of observed breast cancers	SIR	95% CI
1960	Very high/high	117,479	1,908,558	3,185	1.00	0.96–1.03
	Medium	211,325	3,484,538	5,633	1.04	1.01–1.07
	Light	218,970	3,659,085	6,858	1.20	1.17–1.22
	Sedentary	157,130	2,733,432	4,743	1.27	1.23–1.31
1970	Very high/high	234,465	4,148,366	5,223	0.93	0.91–0.96
	Medium	294,799	5,226,171	6,858	1.00	0.98–1:03
	Light	272,794	4,889,584	6,532	1.17	1.15–1.20
	Sedentary	187,212	3,392,443	4,227	1.26	1.22–1.30
1960 and 1970[a]	Very high/high	39,990	690,545	1,141	0.99	0.93–1.05
	Medium	66,456	1,149,743	2,066	1.09	1.04–1.14
	Light	87,960	1,535,617	3,089	1.28	1.24–1.33
	Sedentary	58,930	1,045,697	1,985	1.35	1.29–1.41

[a] Women classified to the same level of occupational physical activity in 1960 and 1970.

Our multivariate analyses, based on internal comparisons within the cohort, are shown in Table 2. In baseline models, adjusted for age and calendar year of follow-up, as well as place of residence, breast cancer risk increased with decreasing level of occupational physical activity, similar to the findings in Table 1. The risk among women classified as holding sedentary jobs in both 1960 and 1970 was between 20% and 40% higher than that in women estimated as having the physically most demanding jobs. Women who switched from the highest to the lowest category of occupational physical activity between 1960 and 1970 had a relative risk of 1.4 (95% CI 1.1–1.9) compared with those who remained in the highest category. In contrast, the risk among women who switched from sedentary in 1960 to high in 1970 was similar to the risk among women with the highest occupational activity level in both 1960 and 1970 (RR = 0.9, 95% CI 0.6–1.2).

Adjustment for socioeconomic status eliminated the association between occupational physical activity and breast cancer risk almost completely; no significant differences were observed in the risk for breast cancer between different occupational physical activity groups (Table 2). When the risk estimates were calculated for the different levels of socioeconomic status in the baseline models, women in the highest social class were at about 30% higher risk for breast cancer than women in the lowest social class. Adjustment for occupational physical activity attenuated these trends only marginally (Table 2). The Spearman correlation coefficient between occupational physical activity and social class scores was 0.61, 0.63, and 0.41 in the three cohorts, respectively. Addition of either occupational physical activity or socioeconomic status to the baseline Poisson regression model improved the model fit significantly. This improvement was greater after the addition of socioeconomic status compared to occupational physical activity (reduction in deviance 141 and 70, respectively – with 3 degrees of freedom – among women classified as having the same level of occupational physical activity in both 1960 and 1970). Addition of physical activity to a model including socioeconomic status, however, did not significantly improve the model fit ($p = 0.35$). In contrast, when socioeconomic status was added to a model including occupational physical activity, the improvement was considerable (reduction in deviance 75; $p < 0.0001$).

We explored relative risk for breast cancer by age at follow-up in the cohort including women classified as having the same level of occupational physical activity in both 1960 and 1970. Without adjustment for socioeconomic status, the inverse association with occupational physical activity was clearest at ages 50–69 years (Table 3). After further adjustment for socioeconomic status an attenuated, albeit statistically significant, trend was confined to women aged 50–59 years (Table 3). However, in the 1960 census cohort and the one from 1970 (with women who did not necessarily have the same level of occupational physical activity in both

Table 2. Relative risk (RR) with 95% confidence interval (CI) for cancer of the breast by estimated physical activity and socioeconomic status in 1960 and 1970. Results obtained by Poisson regression

Variable	Census 1960				Census 1970				Census 1960 and 1970			
	RR[a]	95% CI	RR[b]	95% CI	RR[a]	95% CI	RR[b]	95% CI	RR[a]	95% CI	RR[b]	95% CI
Occupational physical activity												
High/very high	1.0		1.0		1.0		1.0		1.0		1.0	
Medium	1.1	1.0–1.1	1.0	1.0–1.1	1.1	1.0–1.1	1.0	1.0–1.1	1.1	1.0–1.2	1.0	0.9–1.1
Low	1.2	1.2–1.3	1.1	1.0–1.1	1.2	1.2–1.3	1.1	1.0–1.1	1.3	1.2–1.4	1.1	1.0–1.2
Sedentary	1.3	1.2–1.3	1.1	1.0–1.1	1.3	1.3–1.4	1.1	1.0–1.2	1.3	1.2–1.4	1.1	1.0–1.2
p-value for trend	< 0.001		0.01			< 0.001	0.001		< 0.001		0.1	
Socioeconomic status												
Unskilled blue-collar[c]	1.0		1.0		1.0		1.0		1.0		1.0	
Skilled blue-collar[d]	1.0	1.0–1.1	1.0	0.9–1.1	1.1	1.0–1.1	1.0	1.0–1.1	1.1	1.0–1.2	1.1	1.0–1.2
Unskilled white-collar[e]	1.2	1.2–1.3	1.2	1.1–1.2	1.3	1.2–1.3	1.2	1.1–1.3	1.3	1.2–1.4	1.3	1.1–1.4
Skilled white-collar[f]	1.3	1.2–1.3	1.2	1.2–1.3	1.3	1.3–1.4	1.3	1.2–1.3	1.4	1.3–1.4	1.3	1.3–1.4
p-value for trend	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

[a] Relative risk adjusted for age by 5-years intervals, calendar year of follow-up by year, and place of residence.

[b] Relative risk adjusted for age by 5-year intervals, calendar year of follow-up by year, place of residence, socioeconomic status (in the analysis of occupational physical activity), or physical activity (in the analysis of socioeconomic status).

[c] Manual workers with less than 2 years of education after primary school (*e.g.*, carpenter, sewer, farmer, glassmaker, housekeeper).

[d] Manual workers with at least 2 years of education after primary school (*e.g.*, dressmaker, baker, barber, locomotive driver, cook).

[e] Non-manual employees with maximum of 2 years of education after primary school (*e.g.*, teller, telephonist, policeman, archivist).

[f] Non-manual employees with more than 2 years of education after primary school (*e.g.*, midwife, fire engineer, physician, priest).

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Table 3. Relative risk (RR) with 95% confidence interval (CI) for cancer of the breast among women with the same estimated occupational physical activity in 1960 and 1970, by age at follow-up

Age at follow-up	Occupational physical activity	Number of cases	No. of person-years	RR[a]	95% CI	RR[b]	95% CI
< 50	Very high/high	171	185,393	1.0	Ref.	1.0	Ref.
	Medium	325	316,312	1.1	0.9–1.4	1.1	0.9–1.3
	Light	587	519,885	1.3	1.1–1.5	1.1	0.9–1.4
	Sedentary	514	458,961	1.2	1.0–1.4	1.0	0.8–1.4
	p-value for trend			0.04		> 0.5	
50–59	Very high/high	254	179,754	1.0	Ref.	1.00	Ref.
	Medium	498	302,514	1.2	1.0–1.4	1.0	0.9–1.2
	Light	921	432,867	1.5	1.3–1.7	1.2	1.0–1.4
	Sedentary	694	309,770	1.5	1.3–1.7	1.3	1.1–1.7
	p-value for trend			< 0.001		0.005	
60–69	Very high/high	412	209,923	1.0	Ref.	1.0	Ref.
	Medium	723	344,822	1.1	1.0–1.2	1.0	0.9–1.1
	Light	941	381,575	1.2	1.1–1.4	1.0	0.9–1.2
	Sedentary	562	204,890	1.3	1.2–1.5	1.0	0.8–1.3
	p-value for trend			< 0.001		> 0.5	
70+	Very high/high	304	115,476	1.0	Ref.	1.0	Ref.
	Medium	520	186,096	1.1	0.9–1.2	1.0	0.9–1.2
	Light	640	201,290	1.2	1.1–1.4	1.00	0.9–1.2
	Sedentary	215	72,076	1.2	1.0–1.4	0.82	0.6–1.1
	p-value for trend			0.01		0.5	

[a] Relative risk adjusted for age by 5-year intervals, place of residence, and calendar year of follow-up.
[b] Relative risk adjusted for age by 5-year intervals, place of residence, calendar year of follow-up, and socioeconomic status.

censuses), the corresponding trend was not statistically significant; the risk gradient between the most physically active and those most sedentary was 11% and 10% in the 1960 and 1970 census cohorts, respectively.

Among women with the same level of occupational physical activity in both censuses we also explored the risks by age at start of follow-up. The results were statistically unstable among women under 39 years of age. Among women older than 40 years the risk increased monotonically with decreasing level of estimated occupational physical activity, being 30–40% higher in the lowest activity category than in the highest. In all age groups, however, the trend vanished after adjustment for socioeconomic status, and no single risk estimate remained statistically significantly different from the null effect of 1 (data not shown).

In the same subcohort, we finally explored the risk among women aged 50–59 at follow-up, considering different ages at entry to the cohort. The results were unstable among women aged under 40 years at start of follow-up. Among women who were 40–50 years of age at entry to the cohort and 50–59 years at follow-up, the risk was 40% higher in the lowest occupational activity category than in the highest (95% CI 7–84%) even after adjustment for socioeconomic status.

Discussion

Our data provide some, albeit weak, support to the hypothesis that occupational physical activity reduces a woman's risk for breast cancer. If such a protective effect exists, it is likely to be strongest among postmenopausal women who have been physically active in their occupation for most of their lives, particularly between 30 and 50 years of age. After age 60, when the occupational physical demands are usually alleviated, the effect seems to wear off. Admittedly, our measure of occupational physical activity was crude, entailing misclassification and underestimation of any true association [51]. However, our validation study indicated a reasonable agreement between job title-derived and self-reported occupational physical activity, and a clear protective effect of occupational physical activity, unconfounded by socioeconomic status, on endometrial cancer was observed in the same cohort of Swedish women [47].

The population-based cohort design with reporting of occupations before the occurrence of any outcome, and complete long-term follow-up of large numbers of working women are unique characteristics of this study. The repeated exposure assessment enabled us to differentiate between women with stable physical activity and

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those who switched from one level to another. The external validity of our data should be high because *all* Swedish women with the studied occupations were analyzed. Changes in occupational physical activity after 1970 may have affected our results. However, since women in the cohort encompassing women with the same level of occupational physical activity in both 1960 and 1970 censuses remained in the same occupational physical activity category for at least 10 years, it is unlikely that a large proportion changed their physical activity at work during the follow-up.

Information about physical activity during leisure time was not available in our study. Such exercise may bias our risk estimates in an unpredictable direction. As discussed elsewhere [47], the true association would be overestimated if women with sedentary jobs were less physically active, and attenuated if they were more physically active after work than women with more strenuous occupations. The latter of these alternatives is more likely, but reliable population-based data on leisure-time activity in different occupational groups is lacking. In any case, it is unlikely that work–leisure differences in physical activity could conceal a trend between physical activity and cancer risk, particularly since the time spent at work usually exceeds that devoted to leisure-time physical exercise substantially.

Before adjustment for socioeconomic status we noted a modest but statistically significant inverse association between occupational physical activity and risk for breast cancer at all ages, although strongest among women aged 50–59 years. The strength of the association diminished after retirement, and also after change to a more physically demanding job. However, adjustment for socioeconomic status eliminated the overall association between physical activity and breast cancer, indicating substantial confounding by this factor. While socioeconomic status is not a meaningful biological exposure *per se*, we lack data on specific risk factors accounting for this confounding. However, several established breast cancer risk factors [52] such as parity, age at first birth, age at menarche, body mass index, and use of replacement hormones are known to differ by socioeconomic status [53, 54]. Utilization of mammography would be another concern for confounding if there is an association between utilization of mammography screening and socioeconomic status or occupational physical activity. Introduction of diagnostic mammography in Sweden was initiated in the 1970s, and of population-based in the late 1980s. However, preliminary results of an ongoing study at our department exploring possible associations between socioeconomic status and mammography screening attendance in Sweden revealed no significant relationship between these two factors (personal communication). After adjustment for socioeconomic status, the association of occupational physical activity and breast cancer risk remained significant only among women aged 50–59 years and was strongest among women aged 55–59 who were physically active between 30 and 50 years of age. Chance may explain this finding confined to only one of the three cohorts analyzed. Alternatively, a true protective effect of occupational physical activity may be confined to postmenopausal women. The persisting association among women closest to retirement might also occur because they were oldest and thus had the largest proportion of their working career when heavy manual work operations had not yet been replaced by automated processes. Hence, their range of exposure is likely wider than that in the younger age groups.

From eleven studies [2, 5, 7–11, 14, 19, 22, 24] that considered the relationship specifically between occupational physical activity and breast cancer risk, three [2, 10, 22] reported a significant inverse association, seven others reported non-significant trends [5, 7–9, 14, 19, 24], and one [24] reported no relationship. Only two of these studies adjusted for socioeconomic status [8, 9], and no association persisted after such adjustment. Five previous studies [4, 11, 19, 20, 55] evaluated combined measures of recreational and occupational physical activity. In one case–control [19] and two cohort studies [20, 55], a similar inverse relationship with breast cancer risk was reported for both recreational and occupational physical activity. In contrast, in one of the studies [11], the increased risk for breast cancer was observed for highest *versus* lowest level of all combinations for leisure-time and occupational physical activity.

Eighteen studies [1, 3, 5, 6, 11–13, 15–19, 21–23, 25, 26, 27], which examined the relationship between recreational physical activity and breast cancer risk, have produced inconsistent results. While the majority of these studies [1, 12, 13, 15–19, 21, 22, 27] reported a reduced risk for breast cancer among women with high leisure-time physical activity, only five described significant results [12, 13, 16, 22, 27]. It is not clear whether the possible protective effect was restricted to premenopausal or postmenopausal cancer or whether it applied to all women. Moreover, no consistent dose–response relationship was observed across these studies. This lack of consistency may partly derive from the fact that leisure-time physical activity, as opposed to occupational physical activity, rarely accounts for more than a few hours per week. Moreover, leisure-time physical activity may be exposed more to confounding by life-style factors than occupational activity.

A protective effect of physical activity is biologically plausible. Plasma estrogen levels are higher in breast

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cancer cases [31], while physical activity lowers a woman's level of circulating estrogen [28, 56]. Physical activity also prevents weight gain and reduces body fat [29] and consequently may decrease the amount of estrone, the major source of estrogens in postmenopausal women, through aromatization [57]. However, the interplay between physical activity, reproductive factors, body weight, and dietary habits is intricate and remains incompletely understood.

We conclude that the link between physical activity and breast cancer risk remains uncertain and that confounding by factors related to socioeconomic status, such as characteristics of reproductive life, may be a concern when interpreting observed associations. Hence, more studies are needed to unveil the interrelationships between physical activity, known breast cancer risk factors, and breast cancer risk.

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References

1. Frisch RE, Wyshak G, Albright NL, *et al.* (1987) Lower lifetime occurrence of breast cancer and cancers of the reproductive system among former college athletes. *Am J Clin Nutr* **45** (1 Suppl.): 328–335.
2. Vena JE, Graham S, Zielezny M, Brasure J, Swanson MK (1987) Occupational exercise and risk of cancer. *Am J Clin Nutr* **45** (1 Suppl.): 318–327.
3. Paffenbarger RS, Hyde RT, Wing AL (1987) Physical activity and incidence of cancer in diverse populations: a preliminary report. *Am J Clin Nutr* **45**: 312–317.
4. Garnfinkel L, Stellman SD (1988) Mortality by relative weight and exercise. *Cancer* **62**: 1844–1850.
5. Albanes D, Blair A, Taylor P (1989) Physical activity and risk of cancer in the NHANES I population. *Am J Public Health* **79**: 744–750.
6. Paffenbarger RS, Lee IM, Wing AL (1992) The influence of physical activity on the incidence of site-specific cancers in college alumni. In: Jacobs MM, ed. *Exercise, Calories, Fat, and Cancer.* New York: Plenum Press, pp. 7–15.
7. Vihko VJ, Apter DL, Pukkala EI, Oinonen MT, Hakulinen TR, Vihko RK (1992) Risk of breast cancer among female teachers of physical education and languages. *Acta Oncol* **31**: 201—204.
8. Pukkala E, Poskiparta M, Apter D, Vihko V (1993) Life-long physical activity and cancer risk among Finnish female teachers. *Eur J Cancer Prev* **2**: 369–376.
9. Dosemeci M, Hayes RB, Vetter R, *et al.* (1993) Occupational physical activity, socioeconomic status, and risks of 15 cancer sites in Turkey. *Cancer Causes Control* **4**: 313–321.
10. Zheng W, Shu XO, McLaughlin JK, Chow WH, Gao YT, Blot WJ (1993) Occupational physical activity and the incidence of cancer of the breast, corpus uteri, and ovary in Shanghai. *Cancer* **71**: 3620–3624.
11. Dorgan JF, Brown C, Barrett M, *et al.* (1994) Physical activity and risk of breast cancer in the Framingham Heart Study. *Am J Epidemiol* **39**: 662–669.
12. Bernstein L, Henderson BE, Hanisch R, Sullivan-Halley J, Ross RK (1994) Physical exercise and reduced risk of breast cancer in young women. *J Natl Cancer Inst* **86**: 1403–1408.
13. Hirose K, Tajima K, Hamajima N, *et al.* (1995) A large scale, hospital-based case–control study of risk factors of breast cancer according to menopausal status. *Jpn J Cancer Res* **86**: 146–154.
14. Steenland K, Nowlin S, Palu S (1995) Cancer incidence in the National Health and Nutrition Survey. I. Follow-up data: diabetes, cholesterol, pulse, and physical activity. *Cancer Epidemiol Biomarkers Prev* **4**: 807–811.
15. Friedenreich CM, Rohan TE (1995) Physical activity and risk of breast cancer. *Eur J Cancer Prev* **4**: 145–151.
16. Mittendorf R, Longnecker MP, Newcomb PA, *et al.* (1995) Strenuous physical activity in young adulthood and risk of breast cancer (United States). *Cancer Causes Control* **6**: 347–353.
17. Taioli E, Barone J, Wynder EL (1995) A case–control study on breast cancer and body mass. The American Health Foundation, Division of Epidemiology. *Eur J Cancer* **31A**: 723–728.
18. McTiernan A, Stanford JL, Weiss NS, Daling JR, Voigt LF (1996) Occurrence of breast cancer in relation to recreational exercise in women age 50–64 years. *Epidemiology* **7**: 598–604.
19. D'Avanzo B, Nanni O, La Vecchia C, *et al.* (1996) Physical activity and breast cancer risk. *Cancer Epidemiol Biomarkers Prev* **5**: 155–160.
20. Michels-Blanck H, Byers T, Mokdad AH, Will JC, Calle EE (1996) Menstrual patterns and breast cancer mortality in a large US cohort. *Epidemiology* **7**: 543–546.
21. Hu YH, Nagata C, Shimizu H, Kaneda N, Kashiki Y (1997) Association of body mass index, physical activity, and reproductive histories with breast cancer: a case control study in Gifu, Japan. *Breast Cancer Res Treat* **43**: 65–72.
22. Thune I, Brenn T, Lund E, Gaard M (1997) Physical activity and the risk of breast cancer. *N Engl J Med* **336**: 1269–1275.
23. Chen CL, White E, Malone KE, Daling JR (1997) Leisure-time physical activity in relation to breast cancer among young women (Washington, United States). *Cancer Causes Control* **8**: 77–84.
24. Coogan PF, Newcomb PA, Clapp RW, Trentham-Dietz A, Baron JA, Longnecker MP (1997) Physical activity in usual occupation and risk of breast cancer (United States). *Cancer Causes Control* **8**: 626–631.
25. Gammon MD, Schoenberg JB, Britton J, *et al.* (1998) Recreational physical activity and breast cancer risk among women under age 45 years. *Am J Epidemiol* **147**: 273–280.
26. Rockhill B, Willet WC, Hunter DJ, *et al.* (1998) Physical activity and breast cancer risk in a cohort of young women. *J Natl Cancer Inst* **90**: 1155–1160.
27. Carpenter CL, Ross R, Paginini-Hill A, Bernstein L (1996) Lifetime physical activity and breast cancer risk among postmenopausal women (abstract). *Am J Epidemiol* **143**: S87.
28. Nelson ME, Meredith CN, Dawson-Hughes B, Evans WJ (1988) Hormone and bone mineral status in endurance-trained and sedentary postmenopausal women. *J Clin Endocrinol Metab* **66**: 927–933.
29. King AC, Tribble DL (1991) The role of exercise in weight regulation in nonatheletes. *Sports Med* **11**: 331–349.

30. Sellers TA, Gapstur SM, Potter JD, Kushi LH, Bostick RM, Folsom AR (1993) Association of body fat distribution and family histories of breast and ovarian cancer risk of postmenopausal breast cancer. *Am J Epidemiol* **138**: 799–803.
31. Toniolo PG, Levitz M, Zeleniuch-Jacquotte A, *et al.* (1995) A prospective study of endogenous estrogens and breast cancer in postmenopausal women. *J Natl Cancer Inst* **87**: 190–197.
32. Bullen BA, Skrinar GS, Beitins IZ, von Mering G, Turnbull BA, McArthur JW (1985) Induction of menstrual disorders by strenuous exercise in untrained women. *N Engl J Med* **312**: 1349–1353.
33. Ellison PT, Lager C (1986) Moderate recreational running is associated with lowered salivary progesterone profiles in women. *Am J Obstet Gynecol.* **154**: 1000–1003.
34. Bernstein L, Ross RK, Lobo RA, Hanisch R, Krailo MD, Henderson BE (1987) The effects of moderate physical activity on menstrual cycle patterns in adolescence: implications for breast cancer prevention. *Br J Cancer* **55**: 681–685.
35. Broocks A, Pirke KM, Schweiger U, *et al.* (1990) Cyclic ovarian function in recreational athletes. *J Appl Physiol* **68**: 2083–2086.
36. Dorgan JF (1998) Physical activity and breast cancer: is there a link? *J Natl Cancer Inst* **90**: 1116–1117.
37. Official Statistics of Sweden (1975) *Census of the Population and Housing in 1970.* Part 13: *Occupation and Education.* Stockholm.
38. Lunde AS, Lundeborg S, Lettenström R, Huebner J (1980) *The Person-Number Systems of Sweden, Norway, Denmark, and Israel.* Department of Health and Human Services Publ. No. (PHS) 80-1358. Vital and Health Statistics, Series 2, No. 84, pp. 5–11. Hyattsville, MD: National Center for Health Statistics.
39. Official Statistics of Sweden (1974) *Population and Housing Census* 1970. Part 12: *Report on the Planning and Processing of the Population and Housing Census.* Lund.
40. Official Statistics of Sweden (1965) *Census of the Population and Housing in 1960: Report on the Planning and Processing of the Census of the Population and Housing.* Stockholm.
41. Mattson B (1977) *The Completeness of Registration in the Swedish Cancer Register.* Statistical Reports HS 1977. Report No. 15. Stockholm: National Board of Health and Welfare.
42. *Causes of Death 1971–1989* (Yearly Report, in Sweden). Stockholm: Statistics Sweden.
43. *Cancer Miljöregistret 1960–1970.* EPC Rapport 1994:4 Stockholm: Socialstyrelsen.
44. *Official* Statistics of Sweden (1971) *Census of the Population and Housing in 1970*, 1.4. Stockholm: Statistics Sweden.
45. The National Labor Market Board (1965) *The Nordic Occupational Classification System.*
46. International Labor Office (1958) *International Standard Classification of Occupations.* Geneva: International Labor Office.
47. Moradi T, Nyrén O, Bergström R, *et al.* (1998) Risk for endometrial cancer in relation to occupational physical activity: a nationwide cohort study in Sweden. *Int J Cancer* **76**: 665–670.
48. Swedish socioeconomic classification (1995) *Reports on Statistical Co-ordination*, 1982:4. Stockholm: Statistics Sweden.
49. Preston DL, Lubin JH, Pierce DA (1995) EPICURE: Generalized Regression Models for Epidemiologic Data. Seattle, WA: HiroSoft International Corporation.
50. Kleinbaum DG, Kupper LL, Muller KE (1987) *Applied Regression Analysis and Other Multivariable Methods.* Belmont, CA: Duxbury Press.
51. Rothman KJ (1986) *Modern Epidemiology.* Boston. MA: Little, Brown and Company.
52. Schottenfeld D, Fraumeni JF (1996) *Cancer Epidemiology and Prevention*, 2nd edn. New York: Oxford University Press.
53. Kogevinas M, Pearce N, Susser M, Boffetta P (1997) *Social Inequalities and Cancer.* Lyon: IARC Scientific Publications, No. **138**: pp. 285–308.
54. Wamala SP, Wolk A, Orth-Gomér K (1997) Determinants of obesity in relation to socioeconomic status among middle-aged Swedish women. *Prev Med* **26**: 734–744.
55. Thune I, Lund E (1997) Exercise and breast cancer (letter). *N Engl J Med* **337**: 709.
56. Cauley JA, Gutai JP, Kuller LH, LeDonne D, Powell JG (1989) The epidemiology of serum sex hormones in postmenopausal women. *Am J Epidemiol* **129**: 1120–1131.
57. Enriori CL, Reforzo-Membrives J (1984) Peripheral aromatization as a risk factor for breast and endometrial cancer in postmenopausal women: a review. *Gynecol Oncol* **17**: 1–21.

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