

# **Exercise and Reduced Breast Cancer Risk; A Multinational Study**

# Introduction

Many studies have shown that physical activity is associated with reduced risk of breast cancer. However there are inconsistencies in many areas that need to be resolved (Sprague et.al., 2007). Areas of particular interest include further analyses of effect modification by race, menopausal status and cancer characteristics such as receptor status and node involvement.

The present study examines the relationship between recreational physical activity and breast cancer risk in a population based case-control study.

## Study Aim

To examine the association between exercise and risk breast cancer.

# Methods

### **Overview of the Study**

•The Global Epidemiology Study: The Global Epidemiology Study (GES) is a multinational study to assess disease risk factors. Subjects were recruited to the GES from countries including the United States, Tunisia and Poland. The GES is linked to the Global Repository that houses biomaterial. For breast cancer, newly diagnosed subjects provided informed consent and were asked about exercise activity during in-person interviews using the same survey instrument. •Participants: We examined the association between exercise and breast cancer

risk among 1462 breast cancer cases and 4863 cancer-free controls in the Global Epidemiology Study (GES).

### **Design of Current Project**

Participants: 1462 breast cancer cases and 4863 controls (total=6325)

- Inclusion criteria:
- Physical activity data available
- Race of Caucasian-Americans, African-Americans, Hispanic-Americans, Tunisian-Arabs, and Polish-Caucasians (Asians were excluded due to unavailability of controls)

**Covariate data:** Data from the baseline questionnaire and medical assessment included data on age, race, diet, physical activity, cancer family history, cancer histology, cancer stage, tumor receptor status and lymph node involvement.

### **Statistical Analyses:**

•Cross tabulations with Chi square tests and t-tests were conducted to determine the association between cancer status and potential confounders.

•Unconditional logistic regression was used to compute odds ratios (ORs) and 95% confidence intervals (CIs). The variables used in the multivariate analyses were age, pack-years of smoking and BMI as continuous variables and race as a categorical variable.

•Potential confounding of the association between exercise and cancer risk was explored using Spearman rank correlation analyses and multivariate logistic regression models, including stepwise regression models. If the potential confounder caused a >20% change in the  $\beta$  coefficient, it was kept in the model for further analyses.

•All p-values shown are 2-sided.

•All statistical analyses were performed using the software package STATA (STATA Corporation, College Station, TX).

# Results

Table 1. Crossta	bs of Demo	graphics an	d Health	Behavior Inc	dicators						Overall OR (95% CI) [Cases/Controls]	Caucasian-American OR (95% CI) [Cases/Controls]	African-American OR (95% CI) [Cases/Controls]
Characteristic	All Controls (N=4862)	All Cases (N=1463)	P-Value	Caucasian American Controls (N=2406)	Caucasian American Cases (N=973)	P-Value	African American Controls (N=406)	African American Cases (N=88)	P-Value	Exercise (Times/week) Tertile 1: <1 Tertile 2: 1-3 Tertile 3: >3	1.0 (ref) [660/1433] 0.50 (0.42-0.58) [324/1464] 0.48 (0.41-0.55) [446/1951] P <sub>trend</sub> =0.0001	1.0 (ref) [390/580] 0.51 (0.42-0.62) [238/775] 0.46 (0.39-0.56) [317/1042] P <sub>trend</sub> =0.0001	1.0 (ref) [45/86] 0.34 (0.18-0.66) [12/121] 0.21 (0.11-0.39) [21/199] P <sub>trend</sub> =0.0001
Age (Years)* Smoking No Yes	53.5 3240 [66.6%] 1624 [33.4%]	59.3 874 [59.9%] 586 [40.1%]	<0.0001	56.6 [13.1] 1434 [59.6%] 974 [40.4%]	61.08 [13.4] 520 [53.5%] 452 [46.5%]	<0.0001	45.6 [12.2] 176 [43.4%] 230 [56.7%]	56.3 [13.3] 47 [53.4%] 41 [46.6%]	<0.0001 ns	Exercise (Mins/time) Tertile 1: <10 mins Tertile 2: 10-30 mins Tertile 3: >30 mins	1.0 (ref) [675/1525] 0.46 (0.40-0.54) [373/1733] 0.61 (0.53-0.71) [420/1602]	1.0 (ref) [402/634] 0.57 (0.48-0.69) [302/869] 0.51 (0.42-0.62) [274/905]	1.0 (ref) [48/96] 0.28 (0.15-0.51) [22/180] 0.27 (0.14-0.52) [18/130]
Smoking pack years*	5.4 [12.7]	7.8 [15.8]	<0.0001	18.5 [19.7]	21.5 [21.2]	<0.01	10.9 [12.2]	15.4 [13.6]	<0.04		P <sub>trend</sub> =0.0001	P <sub>trend</sub> =0.0001	P <sub>trend</sub> =0.0001
Vegetables (Servs/day)* Fruits (Servs/day)* Red meat (Times/week)*	2.0 [1.2] 1.8 [1.1] 2.7 [1.9]	2.1 [1.2] 1.9 [1.1] 2.6 [1.8]	<0.03 ns ns	2.2 [1.3] 1.9 [1.2] 2.6 [1.9]	2.3 [1.2] 2.0 [1.2] 2.5 [1.8]	ns <0.02 ns	2.3 [1.3] 2.0 [1.5] 3.3 [3.0]	1.7 [1.0] 1.6 [1.3] 2.5 [1.9]	<0.0001 <0.05 <0.005	Exercise (Mins/week) Tertile 1: <30 mins Tertile 2: 30-150 mins Tertile 3: >150 mins	1.0 (ref) [671/1539] 0.47 (0.40-0.54) [325/1579] 0.62 (0.54-0.72) [472/1747] P <sub>trend</sub> =0.0001	1.0 (ref) [398/619] 0.52 (0.43-0.63) [259/832] 0.55 (0.46-0.67) [321/957] P <sub>trend</sub> =0.0001	1.0 (ref) [48/99] 0.31 (0.16-0.57) [20/143] 0.25 (0.14-0.52) [20/164] P <sub>trend</sub> =0.0001
BMI, Kg/m²^	27.5 [6.0]	27.8 [6.1]	<0.03	27.3 [5.9]	27.7 [6.4]	ns	31.0 [7.9]	30.4 [6.9]	ns		Hispanic-American	Tunisian-Arab	Polish-Caucasian
Exercise (Times/week)*	3.0 [2.6]	2.4 [2.7]	<0.0001	3.3 [2.6]	2.6 [2.6]	<0.0001	3.6 [2.7]	2.0 [2.6]	<0.0001		OR (95% CI) [Cases/Controls]	OR (95% CI) [Cases/Controls]	OR (95% CI) [Cases/Controls]
Exercise (Mins/time)*	33.8 [45.1]	27.5 [46.9]	<0.0001	36.0 [44.0]	26.4 [44.6]	<0.0001	38.4 [52.9]	17.1 [24.5]	<0.0003	Exercise (Times/week)			
Exercise (Mins/week)*	154.1 [256.8]	129.3 [260.1]	<0.001	161.6 [246.9]	116.4 [214.7]	<0.0001	187.3 [297.8]	82.0 [155.6]	<0.0016	Tertile 1: <1	1.0 (ref) [32/422]	1.0 (ref) [93/201]	1.0 (ref) [100/144]
Characteristic	Hispanic American Controls (N=1088)	Hispanic American Cases (N=58)	P-Value	Tunisian Arab Controls (N=266)	Tunisian Arab Cases (N=97)	P-Value	Polish Caucasian Controls (N=696)	Polish Caucasian Cases (N=247)	P-Value	Tertile 3: >3 Exercise (Mins/time)	0.68 (0.36-1.3) [15/334] P <sub>trend</sub> =0.14	(-) [0/21] P <sub>trend</sub> =0.009	0.40 (0.27-0.80) [54/196] 0.38 (0.26-0.53) [93/355] P <sub>trend</sub> =0.0001
Age (Years)*	50.1 [15.7]	60.7 [15.3]	<0.0001	43.4 [9.1]	51.4 [10.8]	<0.0000	56.3 [6.5]	56.3 [11.0]	ns	Tertile 1: <10 mins	1.0 (ref) [32/434]	1.0 (ref) [93/200]	1.0 (ref) [100/161]
Smoking No Yes	892 [81.9%] 197 [18.1%]	44 [77.2%] 13 [22.8%]	ns	260 [98.1%] 5 [1.9]	95 [99.0%] 1 [1.0%]	ns	478 [68.7%] 218 [31.3%]	168 [68.0%] 79 [32.0%]	ns	Tertile 3: >30 mins	0.64 (0.35 - 1.16) [16/366] 0.49 (0.21 - 1.14) [8/267] $P_{trend}=0.06$	- () [0/13] 0.32 (0.10-1.01) [4/51] P <sub>trend</sub> =0.03	0.18 (0.11-0.28) [31/280] 0.78 (0.55-1.09) [116/249] P <sub>trend</sub> =0.5
Smoking pack years*	10.5 [14.9]	20.3 [20.7]	<0.03	7.3 [5.0]	6.5 [-]	-	19.0 [11.2]	14.8 [11.8]	<0.006	Tertile 1: <30 mins	1.0 (ref) [32/462]	1.0 (ref) [93/201]	1.0 (ref) [100/158]
Vegetables (Servs/day)	1.7 [1.1]	1.7 [1.0]	ns	1.9 [0.3]	1.7 [0.5]	<0.0000	1.4 [0.7]	1.4 [0.8]	ns	Tertile 2: 30-150 mins	0.64 (0.33-1.26) [13/325]	0.47 (0.15-1.48) [4/37]	0.20 (0.12-0.31) [29/242]
Fruits (Servs/day)*	1.8 [1.1]	2.0 [1.5]	ns	1.9 [0.3]	2.0 [0.2]	ns	1.5 [0.9]	1.4 [0.8]	ns	Tertile 3: >150 mins	$P_{trend} = 0.33$	$P_{trend} = 0.009$	0.64 (0.45-0.89) [118/296] P <sub>trend</sub> =0.059
Red meat (Times/week)*	2.4 [1.9]	3.0 [2.1]	<0.02	1.8 [0.6]	2.1 [0.7]	<0.0005	3.3 [1.6]	3.2 [1.9]	ns				
BMI, Kg/m <sup>2</sup> *	28.0 [6.2]	29.4 [6.0]	ns	24.1 [2.1]	27.0 [3.1]	<0.0000	26.3 [4.0]	27.5 [5.1]	<0.0001	p-value for trend estimated from logistic regres	sion models.		
Exercise (Times/week)*	2.4 [2.5]	2.0 [2.7]	ns	0.7 [1.7]	0.06 [0.3]	<0.0002	3.7 [2.6]	2.9 [2.8]	<0.0001	Odds Ratios adjusted for age, smoking pack-y	ears and BMI. The overall model was also adjusted for race		
Exercise (Mins/time)*	26.3 [40.0]	13.8 [19.9]	<0.02	22.9 [58.2]	2.3 [11.3]	<0.0006	39.5 [43.4]	48.6 [63.4]	<0.01	Figure 1. Breast Cance	r Categories and Exercise (min	utes per week)	
Exercise (Mins/week)*	110.3 [219.1]	67.1 [104.0]	ns	86.4 [336.0]	3.4 [17.3]	<0.02	202.7 [268.6]	257.9 [423.9]	<0.02				
											< 0.005	P<0.0001	P<0.0001

Mean [Standard Deviation]

### Table 2. Body Mass Index and Breast Cancer Risk

Body Mass Index	Overall OR (95% CI) [Cases/Controls]	Caucasian-American OR (95% CI) [Cases/Controls]	African-American OR (95% CI) [Cases/Controls]
Below 18.5 [Underweight] 18.5 to 24.9 [Healthy weight] 25.0 to 29.9 [Overweight] 30 or higher [Obese]	1.30 (0.78-2.18) [24/58] 1.0 (ref) [505/1840] 1.08 (0.93-1.25) [505/1654] 1.19 (1.02-1.39) [434/1313] p-trend=0.0	1.34 (0.74-2.44) [20/33] 1.0 (ref) [363/963] 1.06 (0.88-1.28) [318/745] 1.07 (0.88-1.30) [277/667] p-trend=0.0	1.98 (0.20-19.38) [1/6] 1.0 (ref) [20/90] 1.05 (0.50-2.19) [27/122] 1.02 (0.51-2.06) [40/188] p-trend=0.0
	Hispanic-American OR (95% CI) [Cases/Controls]	Tunisian-Arab OR (95% CI) [Cases/Controls]	Polish-Caucasian OR (95% CI) [Cases/Controls]
Below 18.5 [Underweight] 18.5 to 24.9 [Healthy weight] 25.0 to 29.9 [Overweight] 30 or higher [Obese]	2.25 (0.25-20/16) [1/12] 1.0 (ref) [13/370] 1.37 (0.65-2.92) [19/366] 1.91 (0.93-3.94) [25/341] p-trend=0.0	- (-) [0/0] 1.0 (ref) [23/165] 3.07 (1.70-5.56) [54/100] 76.42 (9.25-631.12) [1/20] p-trend=0.0	0.88 (0.18-4.33) [2/7] 1.0 (ref) [86/252] 0.83 (0.58-1.17) [87/321] 1.81 (1.22-2.67) [72/116] p-trend=0.0

p-value for trend estimated from logistic regression models. Odds Ratios adjusted for age, smoking pack-years and exercise minutes per week. The overall model was also adjusted for race.

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# conclusions

### Table 3. Exercise and Breast Cancer Rick



observed a consistent in reduction breast cancer risk with increased recreational exercise. This reduction in risk was observed in all race groups, with African-Americans benefiting the most. Thirty minutes of exercise per week was sufficient in all race categories to achieve benefit. Body mass index was associated with breast cancer risk in all the race groups combined category and among Polish-Caucasians and Tunisian-Arabs. Risk of all breast cancers, pre-menopausal, peri-menopausal, post-menopausal, receptor positive, receptor negative, node positive and node negative were reduced with recreational exercise.



