Original Article

# Association between breast cancer risk and leisure physical activity in a rural cohort population

**Shelbie D. Stahr[1], Gail A. Runnells[1], Lora J. Rogers[1], Pearl A. McElfish[2], Susan A. Kadlubar[3], L. Joseph Su[1]**

[1]Department of Epidemiology, Fay W. Boozman College of Public Health, University of Arkansas Medical Sciences, Little Rock, AR, USA; [2]University of Arkansas Medical Sciences Northwest, Fayetteville, AR, USA; [3]Department of Environmental and Occupational Health, Fay W. Boozman College of Public Health, University of Arkansas Medical Sciences, Little Rock, AR, USA

*Contributions*: (I) Conception and design: SA Kadlubar, LJ Su; (II) Administrative support: None; (III) Provision of study materials or patients: SA Kadlubar, PA McElfish, GA Runnells; (IV) Collection and assembly of data: GA Runnells, LJ Rogers, PA McElfish; (V) Data analysis and interpretation: SD Stahr, LJ Su; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*Correspondence to:* L. Joseph Su, PhD, MPH. Department of Epidemiology, Fay W. Boozman College of Public Health, University of Arkansas Medical Sciences, Little Rock, AR 72205, USA. Email: ljsu@uams.edu.

**Background:** Physical activity has been identified as a modifiable risk factor for breast cancer. Varying definitions of physical activity have made the evaluation difficult to analyze. In a state with high prevalence of obesity and elevated rates of breast cancer incidence and mortality, physical activity may be an important element for risk reduction. Women's participation in physical activity and the relation to breast cancer incidence has rarely been determined in the southern states where obesity are prevalent.

**Methods:** Associations between various levels of physical activity and incident breast cancer cases among 21,665 subjects residing in Arkansas from 2007–2018 were completed. Multivariate logistic regression was used to estimate the odds ratios (OR) and 95% confidence intervals (95% CI), adjusting for various risk factors such as age, alcohol use, education, region, ethnicity, age at menarche, ever had children, and history of breastfeeding and family history of breast cancer. Stratification on menopausal status was performed to observe any breast cancer differences within the different biological pathways.

**Results:** Among premenopausal subjects, inverse associations were observed among increase time in walking (OR =0.63, 95% CI: 0.36–1.11 and OR =0.47, 95% CI: 0.26–0.83) and overall weekly physical activity (OR =0.89, 95% CI: 0.50–1.57 and OR =0.52, 95% CI: 0.30–0.90) and breast cancer. No association was evident between the risk for breast cancer and physical activity among postmenopausal subjects. The relationship between physical activity and risk for breast cancer differed between menopausal statuses. The most apparent association was seen among premenopausal subjects with an increase in walking (P=0.01).

**Conclusions:** Although physical activity has been demonstrated to have a beneficial effect on breast cancer prevention among postmenopausal women, results from this study do not sufficiently support the hypothesis in this population. Results varied among menopausal status as well as among different definitions of physical activity. Further investigation is needed to identify factors contributing to de-attenuating the relationships.

**Keywords:** Breast neoplasms; physical activity; rural; disparities; cohort

Submitted Apr 19, 2019. Accepted for publication Jun 09, 2019.
doi: 10.21037/tcr.2019.06.18
**View this article at:** http://dx.doi.org/10.21037/tcr.2019.06.18

## Introduction

Breast cancer is the most common cancer for women and encompasses 15% of all new cancer cases in the United States (1). It is the second leading cause of cancer death among women accounting for approximately 41,760 deaths annually (2). Numerous risk factors, both modifiable and nonmodifiable, have been identified for breast cancer risk. Nonmodifiable factors include age, race, menarche, reproductive history, personal breast cancer history, family history/genetic inheritance, and various medical treatments (3-9). A large part of breast cancer risk comes from modifiable risk factors such as reproductive history, sedentary lifestyle, hormone replacements, smoking, stress/anxiety, body weight, alcohol use, and physical activity (3-12). Of these modifiable risk factors, physical activity has been associated with a 20–80% reduction in the risk of breast cancer (3,7,13,14). The American Cancer Society recommends adults participate in a minimum of 150 minutes of moderate or 75 minutes of vigorous physical activity each week (15). Numerous studies have identified inverse associations between physical activity and breast cancer risk (3-8,10,11,13,14,16-33), as well as positive associations between sedentary behaviors and breast cancer risk (10,20,34). Physical activity is also known to have an inverse dose-response relationship with obesity (35). Despite knowing that being physically active and maintaining a healthy lifestyle decreases one's risk for breast cancer, a substantial proportion of American adults remain physically inactive (36) and nearly 30% of adults 18 years and older in the U.S. have been classified as being obese (37) and the trend continues to increase (38). Particularly in the state of Arkansas, the current adult obesity rate as of 2017 was 35%, ranking the state 7$^{th}$ in the nation for obesity (39). Since 1997, the adult obesity rate has increased over the past 27 years (17% *vs.* 35%) (39). With the alarmingly high rate of obesity among Arkansan women, further investigation into the health effects resulting from lack of physical activity is necessary. By identifying preventative strategies such as physical activity, cases of breast cancer as well as obesity rates can be reduced.

Different mechanistic pathways for breast cancer have been proposed for pre- and post-menopausal women. After menopause, estrogen is largely produced in adipose tissue (40). These sex hormones have been identified to stimulate cellular proliferation in the breast; therefore an increase in adipose tissue in postmenopausal women has been identified as an increased risk for breast cancer (6,11,26,29,32,40). An association between lowering various circulating hormones and growth factors in the body and breast cancer development and progression has been identified (41). By preventing obesity and its adverse health outcomes, particularly relating to body's responses to insulin, reduced inflammation and enhanced immune function are anticipated (42). Among premenopausal women, sex hormones are stored in the ovaries, therefore are less influenced by fat deposition, resulting in an inverse association between obesity and breast cancer (40). Given these known differences in breast cancer pathways between pre- and post-menopausal women, this study utilized data obtained from the Arkansas Rural Community Health (ARCH) Study, a largely rural cohort population in the mid-south region of the United States, to evaluate the association between leisure physical activities and breast cancer among pre- and post-menopausal women in Arkansas.

## Methods

The present study used data collected from the Arkansas Rural Community Health (ARCH) Study cohort, formerly known as Spit for the Cure (43,44). Representation from all 75 counties in Arkansas is included in the cohort, as well as an overrepresentation among the African Americans. Although the cohort is racially diverse, education attainment is higher than the state average. The ARCH population was not intended to be representative of the entire female population. Baseline data including socioeconomic status, family and medical history, reproductive health, and physical activity were collected from 26,347 women between the ages of 18 and 100 through various community events. Among these women, 2,333 women were excluded due to reporting having a breast cancer diagnoses at baseline and 339 women were excluded due to missing or error in baseline information regarding breast cancer status. Those who participated at baseline and consented to be re-contacted were mailed a follow-up survey pertaining to their cancer status. Further linkage to the Arkansas Central Cancer Registry was performed annually through December 2018. A total of 193 women were excluded due to follow-up or Arkansas Central Cancer Registry information indicating having a positive breast cancer diagnosis at baseline. Overall, 23,482 women were eligible for the current study based on breast cancer status. 728 individuals were further excluded due to BMI or weight errors in data entry. A total of 823 women were also excluded due to missing or unsure menopausal status. The final dataset consists of 266 incident breast cancer cases and 21,665 non-cases. Among the cases, 77 reported being premenopausal and 189 reported being postmenopausal. Non-cases consisted of 12,128 premenopausal and 9,537 postmenopausal women. Study protocols are approved by the University of Arkansas for Medical Sciences Institutional Review Board.

### *Breast cancer case definitions*

Baseline and follow-up survey data were self-reported, whereas cancer registry linkage results are based on medical

**Table 1** Examples of physical actives by level

| Physical activity level | Example of activity |
|---|---|
| Vigorous activity | Activities such as heavy lifting, digging, aerobics, or fast bicycling |
| Moderate activity | Activities such as carrying light loads, bicycling at a regular pace, or doubles tennis. Does not include walking |
| Walking | This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure |
| Sitting | This includes time spent at work, at home, while doing course work, and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting, or lying down to watch television |

record abstraction and have been adjudicated (45). Subjects were classified as free of breast cancer at baseline if they reported never having a breast cancer diagnosis at baseline and follow-up and do not to appear on the cancer registry linkage. Breast cancer cases were defined as any individual free of breast cancer diagnoses at enrollment and reported breast cancer diagnosis at least one year after they enrolled in the cohort either through cancer registry linkage or self-reported follow-up surveys (n=266). Any subject diagnosed within a year of their baseline survey were excluded (n=78) from the analysis to avoid potential bias due to underdiagnosed breast cancer at enrollment. Only subjects who had a diagnosis date and/or year at least one year after enrollment were included in the analysis. Subjects stating they were free of breast cancer at baseline and at the follow-up survey, responded "no" to ever having breast cancer in the follow-up, and were not identified in the cancer registry linkage were defined as non-cases in the study (n=21,665).

### *Physical activity assessment*

Physical activity information was based on self-report measures at enrollment (21). Three different measurement and quantification tools were utilized to accurately assess physical activity. First, levels of physical activity were categorized within the self-report questionnaire as, "Vigorous Activity", "Moderate Activity", "Walking", and "Sitting", including examples of activities respective to each category. Examples of self-reported activities are provided in *Table 1*. As commonly reported in the literature, walking was separated from moderate activity due to, depending on how brisk, it generally falls into the lower end of the intensity spectrum for most people. It is thus used to investigate the potential health effects separately (46,47). Frequency of each activity level, as well as the duration of activities, was reported. Analyses were performed on each level of physical activity based on a calculation of total weekly minutes performed. The second assessment of physical activity was the overall amount performed calculated by cumulative weekly minutes of activity. This assessment excluded intensity level previously analyzed and utilized total summation of weekly minutes spent engaging in physical activity. The last assessment was defined as a metabolic equivalent of task (MET) score. The MET score was calculated for each individual based on existing literature (13,48-50). A MET is defined as the resting metabolic rate, the amount of oxygen consumed at rest (49,50). Each level of physical activity was categorized based on the amount of energy expended; more intense activities are given a higher numeric value. The calculation for an individual's weekly MET score is as follows:

*Weekly MET score = (weekly minutes spent sitting ×1) + (weekly minutes spent walking ×3.3) + (weekly minutes participating in moderate physical activity ×4) (weekly minutes participating in vigorous physical activity ×8).*

Any subject who reported "None" for the past seven days of any level of physical activity was recorded as "0" for amount of time spent participating in the corresponding level of physical activity. This was applied for all three assessments of physical activity.

### *Other covariates*

Body mass index (BMI) was calculated as: BMI = [weight (kg) ÷ height ($m^2$)]. Subjects with unreliable or outlier data (less than 15 or greater than 50) were removed from the analyses (n=728). Sociodemographic information provided at baseline such as age (continuous), race (categorical), BMI (continuous), alcohol consumption (categorical), education level (categorical), and region (categorical) were included in the examination for potential confounding or effect modification. Race was analyzed as a categorical variable, white/European American (EA), black/African American (AA) and other. In the final stratified models, other racial groups were excluded from the analysis due to insufficient sample size (cases, n=3) and race was analyzed as a dichotomous variable, EA and AA. Region was analyzed as a dichotomous variable as Rural and Urban, classified by the subjects' zip code at baseline using the rural-urban commuting area (RUCA) codes (51). Endogenous and exogenous hormonal factors potentially affecting the risk of breast cancer such as menarche (continuous), menopausal status (yes/no), ever given birth (yes/no), breastfeeding (yes/no), and family history of breast cancer (yes/no/unsure). Family history of breast cancer included the participants' mother, sister, or daughters' breast cancer history. Any recorded family history resulted in a family history of 'yes'. Collection of breast cancer history among male relatives was not collected at baseline, due to the rareness of the disease (52). In the final stratified models, unsure of any family history groups were excluded from the analysis due to insufficient sample size (cases, n=1) and family history was analyzed as a dichotomous variable, yes or no. A composite variable was created to capture parity and breastfeeding history (never gave birth and never breastfed, at least one child and never breastfed, and had at least one child and had breastfed).

### *Statistical analyses*

Differences in patient characteristics between cases and non-cases were evaluated using $\chi^2$ tests for categorical variables, and *t*-tests for continuous variables. Vigorous and moderate physical activity, as well as time spent walking, were categorized into three classes based on the distributions among cases; the first class being those who participated in the activity for less than one hour per week, the midpoint of the remaining values was identified to separate the lower and upper values into two classes. Time spent sitting, overall weekly physical activity, and the metabolic equivalent of task score were categorized based on tertiles, dividing the variables into three equal parts based on their distributions among cases.

Unconditional logistic regression was used to estimate crude and multivariable-adjusted odds ratios (ORs) and 95% confidence intervals (95% CI) to observe associations between increased breast cancer risk and physical activity. Tests for trend were performed by assessing physical activity tertiles as ordinal variables in the logistic regression model to observe their associations with breast cancer. Potential confounding variables for the association between physical activity and breast cancer were included in the multivariable logistic regression models. The most parsimonious model was used to estimate associations with breast cancer and physical activities, with covariates including age, BMI, parity/breastfeeding history, region, family history of breast cancer, and race. Each analysis performed was two-sided with P values of α less than 0.05. All analyses were performed using SAS version 9.3.

## Results

Demographic information consisting of 266 incident breast cancer cases and 21,665 non-cases are summarized in *Table 2* by menopausal status. The majority of subjects self-identified as EA in both premenopausal (case =75.3%; non-case =73.2%) and postmenopausal (case =82.5%; non-case =77.2%) groups. Among premenopausal subjects, approximately 88% of cases completed either some college/technical degree or completion of college or postgraduate degree, while non-case slightly less non-cases (84.5%) received the same level of education. Education level was lower for postmenopausal subjects. Among cases, approximately 80% complete either some college/technical degree or completion of college or postgraduate degree versus 71% non-cases. Among both pre- and postmenopausal subjects, regardless of case status, there were more subjects who were classified as above a normal weight (overweight to severely obese) than at a normal weight (premenopausal: cases =62.4% *vs.* 33.8%, non-cases =58.9% *vs.* 38.2%; postmenopausal: cases =70.9% *vs.* 25.9%, non-case =69.7% *vs.* 27.2%, respectively). For both pre- and post-menopausal women, cases were more likely to have a family history of breast cancer when compared to non-cases (premenopausal: 32.5% *vs.* 12.5%; postmenopausal 29.1% *vs.* 20.6%). Only one case in the dataset was unsure of any family history of breast cancer. The cohort consisted primarily of subjects who had given birth (premenopausal: case =74.0%; non-cases =60.5%) (postmenopausal: case =89.4%; non-cases =86.4%); of those subjects, 49.1% of premenopausal cancer cases breastfeed, compared to 63.7% of premenopausal non-cases, whereas for postmenopausal cases, 48.5% breastfed and 47.4% of non-cases breastfed. Among premenopausal subjects who breastfed, non-cases were more likely to breastfeed at less than 6 months (51.2%) or 6 months to a year (31.1%) compared to cases (50.0% and 25.0% respectively), whereas cases were more likely to breastfeed more than non-cases for greater than one year (25.0% *vs.* 17.0%). Among postmenopausal subjects, non-cases were more likely to breastfeed for less than 6 months

 

**Table 2** Sociodemographic characteristics of the population by breast cancer status

| Characteristics | Premenopausal women | | | | | Postmenopausal women | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Case | | Non-case | | P† | Case | | Non-case | | P† |
| | N=77 | % | N=12,128 | % | | N=189 | % | N=9,537 | % | |
| Race | | | | | 0.20 | | | | | 0.19 |
| CA/White | 58 | 75.3 | 8,876 | 73.2 | | 156 | 82.5 | 7,360 | 77.2 | |
| AA/African American | 19 | 24.7 | 2,776 | 22.9 | | 30 | 15.9 | 1,901 | 19.9 | |
| Other | 0 | 0.0 | 476 | 3.9 | | 3 | 1.6 | 276 | 2.9 | |
| Missing | 0 | 0.0 | 0 | 0.0 | | 0 | 0.0 | 0 | 0.0 | |
| Education | | | | | 0.21 | | | | | 0.05 |
| Less than high school | 0 | 0.0 | 243 | 2.0 | | 8 | 4.2 | 428 | 4.5 | |
| High school graduate or GED | 8 | 10.4 | 1,623 | 13.4 | | 30 | 15.9 | 2,327 | 24.4 | |
| Some college or technical school | 20 | 26.0 | 3,914 | 32.3 | | 73 | 38.6 | 3,134 | 32.9 | |
| College or post graduate | 48 | 62.3 | 6,335 | 52.2 | | 78 | 41.3 | 3,638 | 38.1 | |
| Missing | 1 | 1.3 | 13 | 0.1 | | 0 | 0.0 | 10 | 0.1 | |
| BMI | | | | | 0.56 | | | | | 0.47 |
| Normal weight (18.5–24.9) | 26 | 33.8 | 4,633 | 38.2 | | 49 | 25.9 | 2,597 | 27.2 | |
| Overweight (25–29.9) | 25 | 32.4 | 3,112 | 25.7 | | 51 | 27.0 | 2,948 | 30.9 | |
| Obese (30–39.9) | 18 | 23.4 | 3,202 | 26.4 | | 70 | 37.0 | 3,052 | 32.0 | |
| Severely obese (≥40) | 5 | 6.5 | 824 | 6.8 | | 13 | 6.9 | 644 | 6.8 | |
| Missing | 3 | 3.9 | 357 | 2.9 | | 6 | 3.2 | 296 | 3.1 | |
| Given birth | | | | | 0.02 | | | | | 0.27 |
| No | 20 | 26.0 | 4,704 | 38.8 | | 18 | 9.5 | 1,155 | 12.1 | |
| Yes | 57 | 74.0 | 7,337 | 60.5 | | 169 | 89.4 | 8,244 | 86.4 | |
| Missing | 0 | 0.0 | 87 | 0.7 | | 2 | 1.1 | 138 | 1.5 | |
| Ever breastfeed§ | | | | | 0.02 | | | | | 0.82 |
| No | 29 | 50.9 | 2,640 | 36.0 | | 87 | 51.5 | 4,300 | 52.2 | |
| Yes | 28 | 49.1 | 4,674 | 63.7 | | 82 | 48.5 | 3,909 | 47.4 | |
| Missing | 0 | 0.0 | 23 | 0.3 | | 0 | 0.0 | 35 | 0.4 | |
| Length of breastfeeding¶ | | | | | 0.50 | | | | | 0.47 |
| Less than 6 months | 14 | 50.0 | 2,419 | 51.2 | | 38 | 45.2 | 2,055 | 51.7 | |
| 6 months to 1 year | 7 | 25.0 | 1,471 | 31.1 | | 30 | 35.7 | 1,202 | 30.2 | |
| Greater than 1 year | 7 | 25.0 | 802 | 17.0 | | 14 | 16.7 | 683 | 17.2 | |
| Missing | 0 | 0.0 | 34 | 0.7 | | 2 | 2.4 | 37 | 0.9 | |
| Alcohol use | | | | | 0.28 | | | | | <0.01 |
| Never to once a year | 37 | 48.0 | 5,105 | 42.1 | | 108 | 57.1 | 5,535 | 58.0 | |
| Once a month | 16 | 20.8 | 3,518 | 29.0 | | 27 | 14.3 | 1,801 | 18.9 | |
| Once a week to several times a week | 23 | 29.9 | 3,257 | 26.9 | | 35 | 18.5 | 1,850 | 19.4 | |
| Every day | 0 | 0.0 | 171 | 1.4 | | 14 | 7.4 | 291 | 3.1 | |
| Missing | 1 | 1.3 | 77 | 0.6 | | 5 | 2.7 | 60 | 0.6 | |

**Table 2** *(continued)*

 

**Table 2** *(continued)*

| Characteristics | Premenopausal women | | | | | Postmenopausal women | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Case | | Non-case | | P† | Case | | Non-case | | P† |
| | N=77 | % | N=12,128 | % | | N=189 | % | N=9,537 | % | |
| Region | | | | | 0.02 | | | | | <0.01 |
| Urban | 42 | 54.5 | 4,904 | 40.4 | | 108 | 57.1 | 3,844 | 40.3 | |
| Rural | 35 | 45.5 | 6,961 | 57.4 | | 81 | 42.9 | 5,557 | 58.3 | |
| Missing | 0 | 0.0 | 263 | 2.2 | | 0 | 0.0 | 136 | 1.4 | |
| Breastfeeding and children | | | | | <0.01 | | | | | 0.52 |
| No children and do not breastfeed | 20 | 26.0 | 4,704 | 38.8 | | 18 | 9.5 | 1,155 | 12.1 | |
| Have children and do not breastfeed | 29 | 37.7 | 2,640 | 21.8 | | 87 | 46.0 | 4,300 | 45.1 | |
| Have children and breastfeed | 28 | 36.3 | 4,674 | 38.5 | | 82 | 43.4 | 3,909 | 41.0 | |
| Missing | 0 | 0.0 | 110 | 0.9 | | 2 | 1.1 | 173 | 1.8 | |
| Family history of breast cancer | | | | | <0.01 | | | | | <0.01 |
| No | 52 | 67.5 | 10,358 | 85.4 | | 133 | 70.4 | 7,391 | 77.5 | |
| Yes | 25 | 32.5 | 1,515 | 12.5 | | 55 | 29.1 | 1,964 | 20.6 | |
| Unsure | 0 | 0.0 | 255 | 2.1 | | 1 | 0.5 | 182 | 1.9 | |
| Missing | 0 | 0.0 | 0 | 0.0 | | 0 | 0.0 | 0 | 0.0 | |
| Age (yrs) (mean, SD) | 42 | 7.6 | 34 | 9.7 | <0.01 | 59 | 10.1 | 56 | 10.6 | <0.01 |
| Missing | 1 | | 61 | | | 0 | | 32 | | |
| BMI (mean, SD) | 28.4 | 6.3 | 28.3 | 6.8 | 0.90 | 29.5 | 6.2 | 29.3 | 6.4 | 0.69 |
| Missing | 0 | | 156 | | | 3 | | 114 | | |
| Menarche (yrs) (mean, SD) | 12.9 | 1.7 | 12.4 | 1.7 | 0.05 | 12.3 | 1.6 | 12.5 | 1.7 | 0.07 |
| Missing | 0 | | 162 | | | 1 | | 157 | | |
| Number of Children§ (mean, SD) | 2 | 1.1 | 2 | 1.2 | 0.42 | 2 | 1.2 | 3 | 1.4 | 0.81 |
| Missing | 2 | | 145 | | | 2 | | 145 | | |

†, Chi-square test for categorical variables (including 'missing'); ‡, *t*-test for continuous variables; §, when ever given birth = 'yes'; ¶, when breastfeeding = 'yes'. lbs, pounds; yrs, years; SD, standard deviation.

(51.7%) and greater than one year (17.2%) compared to cases (45.2% and 16.7% respectively), and cases were more likely to breastfeed 6 months to one year (35.7%) compared to non-cases (30.2%). Regardless of case or menopausal status, the majority of subjects drank alcohol never to once a year, and the least amount of subjects drank every day. Cases in both pre- and postmenopausal groups are more likely to reside in urban areas (54.6% and 57.1%), and non-cases are more likely to reside in rural areas (57.4% and 58.3%). Premenopausal non-cases are more likely to not have children and not breastfeed (38.8% *vs.* 26.0%) and have at least one child and breastfeed (38.5% *vs.* 36.4%) when compared to non-cases. Premenopausal cases are however more likely to have at least one child and not breastfeed when compared to non-cases (37.7% *vs.* 21.8%). Different patterns are seen among postmenopausal subjects; non-cases are more likely to not have children and not breastfeed than cases (12.1% *vs.* 9.5%), and cases are more likely to have at least one child and not breastfeed (46.0% *vs.* 45.1%) as well as have at least one child and breastfeed (43.4% *vs.* 41.0%) compared to non-cases. Mean age of cases (42 yrs) was eight years older than non-cases (34 yrs) among premenopausal subjects. Among postmenopausal subjects; mean age for cases (59 yrs) was three years older than non-cases (56 yrs).

The results of the logistic regression models assessing the association between various forms of physical activity and breast cancer risk are summarized in *Tables 3* and *4*. For the models analyzing vigorous and moderate physical activity,

 

**Table 3** Odds ratios and 95% confidence intervals for association between different measurements of physical activity and breast cancer among premenopausal women

| Physical activity type | Unadjusted | | | | | Adjusted[a] | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Case | Non-case | OR | 95% CI | P | Case | Non-case | OR | 95% CI | P |
| Vigorous physical activity | N=75 | N=11,404 | | | 0.05 | N=74 | N=10,673 | | | 0.18 |
| <1 hour/week | 44 | 4,855 | 1.00 | Ref. | | 43 | 4,536 | 1.00 | Ref. | |
| ≥1 to 3.5 hours/week | 16 | 4,115 | 0.43 | 0.24–0.76 | | 16 | 3,876 | 0.51 | 0.29–0.92 | |
| >3.5 hours/week | 15 | 2,434 | 0.68 | 0.38–1.22 | | 15 | 2,261 | 0.79 | 0.43–1.44 | |
| Moderate physical activity | N=71 | N=11,195 | | | 0.60 | N=71 | N=10,494 | | | 0.84 |
| <1 hour/week | 23 | 3,795 | 1.00 | Ref. | | 23 | 3,525 | 1.00 | Ref. | |
| ≥1 to 2.1 hours/week | 24 | 2,833 | 1.40 | 0.79–2.48 | | 24 | 2,674 | 1.55 | 0.86–2.77 | |
| >2.1 hours/week | 24 | 4,567 | 0.87 | 0.49–1.54 | | 24 | 4,295 | 0.96 | 0.54–1.71 | |
| Time spent walking | N=72 | N=11,226 | | | <0.01 | N=72 | N=10,510 | | | 0.01 |
| <1 hour/week | 26 | 2,291 | 1.00 | Ref. | | 26 | 2,128 | 1.00 | Ref. | |
| ≥1 to 3 hours/week | 24 | 3,787 | 0.56 | 0.32–0.98 | | 24 | 3,572 | 0.63 | 0.36–1.11 | |
| >3 hours/week | 22 | 5,148 | 0.38 | 0.21–0.67 | | 22 | 4,810 | 0.47 | 0.26–0.83 | |
| Time spent sitting | N=76 | N=11,581 | | | 0.80 | N=75 | N=10,841 | | | 0.65 |
| ≤28 hours/week | 29 | 4,694 | 1.00 | Ref. | | 29 | 4,353 | 1.00 | Ref. | |
| >28 to 49 hours/week | 25 | 3,536 | 1.14 | 0.67–1.96 | | 25 | 3,347 | 1.23 | 0.72–2.12 | |
| >49 hours/week | 22 | 3,351 | 1.06 | 0.61–1.85 | | 21 | 3,141 | 1.13 | 0.64–2.01 | |
| Overall weekly physical activity | N=76 | N=11,573 | | | <0.01 | N=75 | N=10,828 | | | 0.02 |
| ≤3 hours/week | 29 | 2,862 | 1.00 | Ref. | | 28 | 2,674 | 1.00 | Ref. | |
| >3 to 7.1 hours/week | 22 | 2,909 | 0.75 | 0.43–1.30 | | 22 | 2,712 | 0.89 | 0.50–1.57 | |
| >7.1 hours/week | 25 | 5,802 | 0.43 | 0.25–0.73 | | 25 | 5,442 | 0.52 | 0.30–0.90 | |
| Metabolic equivalent of task score | N=76 | N=11,646 | | | 0.04 | N=75 | N=10,897 | | | 0.19 |
| ≤3,486 METs | 26 | 3,375 | 1.00 | Ref. | | 26 | 3,138 | 1.00 | Ref. | |
| >3,486 to 4,878 METs | 25 | 2,708 | 1.20 | 0.69–2.08 | | 24 | 2,528 | 1.29 | 0.73–2.26 | |
| >4,878 METs | 25 | 5,563 | 0.58 | 0.34–1.01 | | 25 | 5,231 | 0.69 | 0.40–1.23 | |

[a], adjusted for age, BMI, family history, parity, breastfeeding history, region, and ethnicity. OR, odds ratio; CI, confidence interval; MET, metabolic equivalent of task; BMI, body mass index.

as well as time spend walking a referent of "less than 1 hour/week" was used. Models analyzing time spend sitting, overall weekly physical activity and metabolic equivalent of task score, a referent of the first tertile (lowest frequency of activity) was used.

Limited associations between physical activity and breast cancer risk were observed among premenopausal subjects (*Table 3*). Breast cancer risk was significantly decreased for the second category of vigorous physical activity (OR =0.51, 95% CI: 0.29–0.92) and insignificantly decreased for the third category (OR =0.79, 95% CI: 0.43–1.44) with an insignificant trend (P=0.18). There was no association observed between moderate physical activity and breast cancer. A significant trend was seen in time spent walking (OR =0.63, 95% CI: 0.36–1.11 and OR =0.47, 95% CI: 0.26–0.83) among the second and third category (P=0.01). Breast cancer risk was insignificantly elevated in the second and third tertiles of time spent sitting (OR =1.23, 95% CI: 0.72–2.12 and OR =1.13, 95% CI: 0.64–2.01). Overall weekly physical activity was shown with an insignificant decrease in breast cancer risk for the second tertile (OR =0.89, 95% CI: 0.50–1.57) and a significant decrease in breast cancer risk in the third tertile (OR =0.52, 95% CI: 0.30–0.90), with an overall significant trend (P=0.02). A

**Table 4** Odds ratios and 95% confidence intervals for association between different measurements of physical activity and breast cancer among postmenopausal women

| Physical activity type | Unadjusted | | | | | Adjusted[a] | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Case | Non-case | OR | 95% CI | P | Case | Non-case | OR | 95% CI | P |
| Vigorous physical activity | N=182 | N=8,964 | | | 0.63 | N=176 | N=8,416 | | | 0.53 |
| <1 hour/week | 92 | 4,886 | 1.00 | Ref. | | 89 | 4,591 | 1.00 | Ref. | |
| ≥1 to 2.5 hours/week | 46 | 1,830 | 1.34 | 0.93–1.91 | | 44 | 1,719 | 1.34 | 0.92–1.94 | |
| >2.5 hours/week | 44 | 2,248 | 1.04 | 0.72–1.49 | | 43 | 2,106 | 1.08 | 0.74–1.57 | |
| Moderate physical activity | N=174 | N=8,710 | | | 0.55 | N=168 | N=8,189 | | | 0.46 |
| <1 hour/week | 57 | 3,066 | 1.00 | Ref. | | 55 | 2,860 | 1.00 | Ref. | |
| ≥1 to 4 hours/week | 63 | 3,050 | 1.11 | 0.77–1.60 | | 61 | 2,887 | 1.10 | 0.76–1.58 | |
| >4 hours/week | 54 | 2,594 | 1.12 | 0.77–1.63 | | 52 | 2,442 | 1.16 | 0.79–1.70 | |
| Time spent walking | N=177 | N=8,870 | | | 0.56 | N=172 | N=8,328 | | | 0.52 |
| <1 hour/week | 50 | 2,453 | 1.00 | Ref. | | 49 | 2,294 | 1.00 | Ref. | |
| ≥1 to 3 hours/week | 65 | 3,045 | 1.05 | 0.72–1.52 | | 64 | 2,874 | 1.05 | 0.72–1.53 | |
| >3 hours/week | 62 | 3,372 | 0.90 | 0.62–1.31 | | 59 | 3,160 | 0.89 | 0.60–1.31 | |
| Time spent sitting | N=185 | N=9,183 | | | 0.96 | N=179 | N=8,606 | | | 0.59 |
| ≤28 hours/week | 82 | 4,121 | 1.00 | Ref. | | 80 | 3,863 | 1.00 | Ref. | |
| >28 to 42 hours/week | 45 | 2,163 | 1.05 | 0.72–1.51 | | 42 | 2,021 | 1.02 | 0.70–1.49 | |
| >42 hours/week | 58 | 2,899 | 1.01 | 0.72–1.41 | | 57 | 2,722 | 1.11 | 0.78–1.57 | |
| Overall weekly physical activity | N=186 | N=9,191 | | | 0.56 | N=180 | N=8,613 | | | 0.72 |
| ≤3.4 hours/week | 63 | 2,934 | 1.00 | Ref. | | 62 | 2,736 | 1.00 | Ref. | |
| >3.4 to 11.2 hours/week | 62 | 2,099 | 0.93 | 0.65–1.33 | | 60 | 2,931 | 0.92 | 0.64–1.32 | |
| >11.2 hours/week | 61 | 3,158 | 0.90 | 0.63–1.28 | | 58 | 2,946 | 0.93 | 0.65–1.35 | |
| Metabolic equivalent of task score | N=186 | N=9,255 | | | 0.55 | N=180 | N=8,670 | | | 0.98 |
| ≤3,297 METs | 62 | 2,919 | 1.00 | Ref. | | 59 | 2,733 | 1.00 | Ref. | |
| >3,297 to 5,430 METs | 63 | 3,137 | 0.95 | 0.66–1.35 | | 63 | 2,946 | 1.06 | 0.74–1.53 | |
| >5,430 METs | 61 | 3,199 | 0.90 | 0.63–1.28 | | 58 | 2,991 | 1.01 | 0.70–1.45 | |

[a], adjusted for age, BMI, family history, parity, breastfeeding history, region, and ethnicity. OR, odds ratio; CI, confidence interval; MET, metabolic equivalent of task; BMI, body mass index.

marginally significant decrease in breast cancer risk can be seen in those in the third tertile (OR =0.69, 95% CI: 0.40–1.23) for the MET scores, however the estimates did not decrease monotonically.

Association between breast cancer and physical activity for post-menopausal subjects is summarized in *Table 4*. An insignificant increase in breast cancer risk was seen in vigorous physical activity among the second category (OR =1.34, 95% CI: 0.92–1.94), while minimal difference was seen in the third (OR =1.08, 95% CI: 0.74–1.57). Similarly, minimal difference in risk was seen for the second category (OR =1.10, 95% CI: 0.76–1.58) and an insignificant increase in risk was seen for the third category (OR =1.16, 95% CI: 0.79–1.70) among moderate physical activity. Minimal change in risk in time spent walking was seen between the second or third category (OR =1.05, 95% CI: 0.72–1.53 and OR =0.89, 95% CI: 0.60–1.31, respectively). An insignificant increase in breast cancer risk among the third tertile (OR =1.11, 95% CI: 0.78–1.57) was seen for time spent sitting, although the test for trend was not significant (P=0.59), minimal difference was seen among the second tertile (OR =1.02, 95% CI: 0.70–1.49). Minimal decrease in risk for overall weekly physical activity was seen among the second and third tertiles (OR =0.92, 95% CI: 0.64–1.32 and OR =0.93, 95% CI: 0.65–1.35, respectively) with no apparent trend (P=0.72). Similarly, minimal increase in risk is seen for MET scores among the second and third tertiles (OR =1.06, 95% CI: 0.74–1.53 and OR =1.01, 95% CI: 0.70–1.45, respectively) with no evidence of a trend (P=0.98).

## Discussion

Data from the ARCH study were utilized to examine associations between physical activity and breast cancer risk among EA and AA participants. Associations between physical activity and breast cancer among premenopausal subjects were evident, while the association was less apparent in postmenopausal subjects. Premenopausal subjects were observed to have more congruent associations among assessments that did not require the subject to define their intensity levels of physical activity, such as walking and overall hours of weekly physical activity. These differences observed within premenopausal subjects could be attributed to inaccurate self-reported physical activity. Although self-report questionnaires are one of the most common tools for measuring physical activity, their ability to produce valid and precise measurements is lacking (20,21). These self-reports may vary due to factors such as obesity and level of intensity (21). By asking participants to classify their intensity levels of each category, recall bias may occur as well as overlap between levels of activity intensity. Without requesting subjects to define their physical activities into different intensity levels, we see more significant associations in analyses examining overall amount of physical activity.

While not statistically significant, we observed a reduced risk for breast cancer among premenopausal subjects who participated in more vigorous physical activity. These results may be in part due to an excess amount of strenuous exercise in premenopausal subjects. This high-intensity athletic performance can cause various health abnormalities such as amenorrhea, and delayed menarche (22,29). This has been hypothesized to decrease a premenopausal woman's risk for breast cancer due to the low levels of estrogen circulating in the body (22,29). In most of the previous studies examining breast cancer risk, the populations are largely comprised of postmenopausal subjects; fewer studies examine this relationship exclusively in premenopausal subjects. There is no scientific consensus regarding the intensity of physical activity level, as well as the period of exposure for a reduced risk of breast cancer among premenopausal subjects (29,32). Although the current study does not produce many significant findings on higher intense physical activities, different directions in breast cancer risk can be seen between premenopausal and postmenopausal subjects. These differences may indicate that the previously described pathways of breast cancer differ depending upon menopausal status. In agreement to previous literature, our data, although the majority not statistically significant, suggests physical activity produces a protective effect towards breast cancer among premenopausal subjects.

The present study was unable to establish an association between risk for breast cancer among postmenopausal subjects and physical activity. One hypothesis that may explain the null findings is obesity (7). It is evident in the literature that physical activity is needed to sufficiently reduce adiposity, thus reducing circulating estrogen levels in women postmenopausal (30,32,40). Despite knowing that a decrease in obesity is related to a decreased breast cancer risk, the optimal intensity level to decrease breast cancer risk in postmenopausal women is still under-defined (30). Previous studies have established that obesity has an association with breast cancer risk among postmenopausal subjects (4-8,10,11,23-32,53), particularly a dose-response relationship (30,37). While the current study adjusted for BMI as a confounding factor, given majority of this study cohort are overweight or obese (>60% and 70% among pre- and post-menopausal women, respectively), residual confounding may still occur due to inaccurate self-report measures. A subsequent analysis was carried out among postmenopausal subject, while stratifying among obesity status. However no significant differences were observed (results not shown).

Upon further investigation regarding the relationship between individuals BMI level and their overall amount of physical activity, we observed significant correlation among both premenopausal and postmenopausal subjects (data not shown). Within premenopausal subjects, we observed that as BMI increases, the overall amount of weekly physical activity decreases. A similar relationship was found among postmenopausal subjects, however the association was not as strong. We hypothesize that these differences regarding obesity may partially explain the findings presented in this study that physical activity was inversely associated with breast cancer among premenopausal subjects but not postmenopausal subjects. This may also be in part due to uncontrolled residual confounding (9).

Other explanations may account for the null associations found among breast cancer risk and physical activity observed among postmenopausal subjects. Information on other cancer type besides breast is not a variable at this point. Data collected at baseline as well as follow-up data were recorded using self-reported questionnaires. These responses are at an increased risk for recall bias due to social desirability and cognitive demands of recall (17). This may be particularly true for weight and waist and hip circumferences (20,21,54). These issues can be higher among cases undergoing treatment as well as having treatment-related or disease-related symptoms. Although cases were identified and surveys were collected a minimum of one year before diagnosis, undiagnosed cases may still have disease-related symptoms prior to diagnosis. As a result, individuals may have reflected modified behavior. Questions regarding self-reported physical activity at baseline were asked in regards to days participated and duration of participation. Several participants reported over six hours of vigorous physical activity seven days out of the week. This suggests that these questions are subject to possible misreporting bias (10). This bias could be due to social desirability or different interpretations of the different levels of physical activity among participants. Even though there was no distinction made regarding leisure time *vs.* occupational physical activity in the questionnaire, the literature indicates that there is a distinction between the two (27). Individuals may over or under report based on their occupational status, including or excluding physical activity that is carried out while at place of employment. Results of this study could be biased due to this distinction.

In general, when making comparisons among premenopausal and postmenopausal results, variation can be observed regarding the direction of associations. Overall, the relationship between physical activity and breast cancer among premenopausal subjects produced an inverse association. As the amount of any physical activity increases, the breast cancer risk generally decreases. Among postmenopausal subjects, non-significant direct associations can be seen for nearly all classifications of physical activity. However, among postmenopausal women, these relationships are minuscule. By observing the dissimilar directionality between women of differing menopausal statuses, we hypothesize that there are other unknown factors, particularly among postmenopausal women, that play a role in the risk for breast cancer.

## Conclusions

This study identified that various levels of physical activity are likely to be associated with breast cancer risk among Arkansan women. While results were not established among postmenopausal subjects, more substantial results were found among premenopausal subjects. This study has highlighted that breast cancer risk is not equivalent between women of different menopausal status, and should be investigated individually, particularly regarding the covariate of obesity. While all findings did not provide significant associations, they cannot be ruled out. The lack of concordance in associations between menopausal statuses entails caution for the interpretation of these results. For all women, participation in moderate physical activity is encouraged. With substantial breast cancer incidence in the state of Arkansas, and few established modifiable risk factors are known, further investigation into physical activity is needed to accurately determine the relationship with breast cancer risk among both pre- and postmenopausal women.

## Acknowledgments

*Funding:* This research was supported by a grant from the Arkansas Breast Cancer Research Programs.

## Footnote

*Provenance and Peer Review:* This article was commissioned by the Guest Editors (Hui-Yi Lin, Tung-Sung Tseng) for the series "Population Science in Cancer" published in *Translational Cancer Research*. The article has undergone external peer review.

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr.2019.06.18). The series "Population Science in Cancer" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Study protocols are approved by the University of Arkansas for Medical Sciences Institutional Review Board. Informed consent was waived due to the retrospective nature of the study.

## References


1. Cancer Stat Facts: Common Cancer Sites. In: National Cancer Institute: Surveillance E, and End Results Program.
2. Cancer Facts & Figures 2019. American Cancer Society 2019:76.
3. Hartman SJ, Dunsiger SI, Marcus BH. A pilot study of a physical activity intervention targeted towards women at increased risk for breast cancer. Psychooncology 2013;22:381-7.
4. Hartman TJ, Gapstur SM, Gaudet MM, et al. Dietary Energy Density and Postmenopausal Breast Cancer Incidence in the Cancer Prevention Study II Nutrition Cohort. J Nutr 2016;146:2045-50.
5. Bellocco R, Marrone G, Ye W, et al. A prospective cohort study of the combined effects of physical activity and anthropometric measures on the risk of post-menopausal breast cancer. Eur J Epidemiol 2016;31:395-404.
6. Neilson HK, Farris MS, Stone CR, et al. Moderate-vigorous recreational physical activity and breast cancer risk, stratified by menopause status: a systematic review and meta-analysis. Menopause 2017;24:322-44.
7. Neil-Sztramko SE, Boyle T, Milosevic E, et al. Does obesity modify the relationship between physical activity and breast cancer risk? Breast Cancer Res Treat 2017;166:367-81.
8. Winters S, Martin C, Murphy D, et al. Breast Cancer Epidemiology, Prevention, and Screening. Prog Mol Biol Transl Sci 2017;151:1-32.
9. What Are the Risk Factors for Breast Cancer? In: Division of Cancer Prevention and Control CfDCaP, editor. U.S. Department of Health & Human Services; 2018.
10. Nomura SJO, Dash C, Sheppard VB, et al. Sedentary time and postmenopausal breast cancer incidence. Cancer Causes Control 2017;28:1405-16.
11. van Gemert WA, Iestra JI, Schuit AJ, et al. Design of the SHAPE-2 study: the effect of physical activity, in addition to weight loss, on biomarkers of postmenopausal breast cancer risk. BMC Cancer 2013;13:395.
12. Bagnardi V, Rota M, Botteri E, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. Br J Cancer 2015;112:580-93.
13. Goh J, Kirk EA, Lee SX, et al. Exercise, physical activity and breast cancer: the role of tumor-associated macrophages. Exerc Immunol Rev 2012;18:158-76.
14. Bernat JK, Anderson LB, Parrish-Sprowl J, et al. Exploring the association between dispositional cancer worry, perceived risk, and physical activity among college women. J Am Coll Health 2015;63:216-20.
15. Summary of the ACS Guidelines on Nutrition and Physical Activity. Society TAC. 2016.
16. Mittendorf R, Longnecker MP, Newcomb PA, et al. Strenuous physical activity in young adulthood and risk of breast cancer (United States). Cancer Causes Control 1995;6:347-53.
17. Hills AP, Mokhtar N, Byrne NM. Assessment of physical activity and energy expenditure: an overview of objective measures. Front Nutr 2014;1:5.
18. Moore SC, Lee IM, Weiderpass E, et al. Association of Leisure-Time Physical Activity With Risk of 26 Types of Cancer in 1.44 Million Adults. JAMA Intern Med 2016;176:816-25.
19. Chlebowski RT. Nutrition and physical activity influence on breast cancer incidence and outcome. Breast 2013;22 Suppl 2:S30-7.
20. Mazzoni AS, Nordin K, Berntsen S, et al. Comparison between logbook-reported and objectively-assessed physical activity and sedentary time in breast cancer patients: an agreement study. BMC Sports Sci Med Rehabil 2017;9:8.
21. Wanner M, Richard A, Martin B, et al. Associations between self-reported and objectively measured physical activity, sedentary behavior and overweight/obesity in NHANES 2003-2006. Int J Obes (Lond) 2017;41:186-93.
22. Bullen BA, Skrinar GS, Beitins IZ, et al. Induction of menstrual disorders by strenuous exercise in untrained women. N Engl J Med 1985;312:1349-53.
23. McTiernan A, Stanford JL, Weiss NS, et al. Occurrence of breast cancer in relation to recreational exercise in women age 50-64 years. Epidemiology 1996;7:598-604.
24. Schmidt ME, Steindorf K, Mutschelknauss E, et al. Physical activity and postmenopausal breast cancer: effect modification by breast cancer subtypes and effective periods in life. Cancer Epidemiol Biomarkers Prev 2008;17:3402-10.
25. Brinton LA, Smith L, Gierach GL, et al. Breast cancer risk in older women: results from the NIH-AARP Diet and Health Study. Cancer Causes Control 2014;25:843-57.
26. Suzuki R, Iwasaki M, Kasuga Y, et al. Leisure-time physical activity and breast cancer risk by hormone receptor status: effective life periods and exercise intensity. Cancer Causes Control 2010;21:1787-98.
27. George SM, Irwin ML, Matthews CE, et al. Beyond recreational physical activity: examining occupational and


 

household activity, transportation activity, and sedentary behavior in relation to postmenopausal breast cancer risk. Am J Public Health 2010;100:2288-95.
28. McTiernan A. Exercise and breast cancer--time to get moving? N Engl J Med 1997;336:1311-2.
29. Rockhill B, Willett WC, Hunter DJ, et al. Physical activity and breast cancer risk in a cohort of young women. J Natl Cancer Inst 1998;90:1155-60.
30. Goncalves AK, Dantas Florencio GL, Maisonnette de Atayde Silva MJ, et al. Effects of physical activity on breast cancer prevention: a systematic review. J Phys Act Health 2014;11:445-54.
31. Ekenga CC, Parks CG, Sandler DP. A prospective study of occupational physical activity and breast cancer risk. Cancer Causes Control 2015;26:1779-89.
32. Kruk J. Intensity and timing in life of recreational physical activity in relation to breast cancer risk among pre- and postmenopausal women. J Sports Sci Med 2010;9:311-9.
33. Arem H, Moore SC, Patel A, et al. Leisure time physical activity and mortality: a detailed pooled analysis of the dose-response relationship. JAMA Intern Med 2015;175:959-67.
34. Arem H, Pfeiffer RM, Engels EA, et al. Pre- and postdiagnosis physical activity, television viewing, and mortality among patients with colorectal cancer in the National Institutes of Health-AARP Diet and Health Study. J Clin Oncol 2015;33:180-8.
35. Jakicic JM, Davis KK. Obesity and physical activity. Psychiatr Clin North Am 2011;34:829-40.
36. An R, Xiang X, Yang Y, et al. Mapping the Prevalence of Physical Inactivity in U.S. States, 1984-2015. PLoS One 2016;11:e0168175.
37. Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion, Division of Nutrition, Physical Activity, and Obesity. Data, Trend and Maps.
38. The State of Obesity Better Policies for a Healthier America. Robert Wood Johnson Foundation. Available online: https://www.stateofobesity.org/obesity-rates-trends-overview/
39. The State of Obesity in Arkansas. 2017. Available online: https://www.stateofobesity.org/states/ar/
40. Rose DP, Vona-Davis L. Interaction between menopausal status and obesity in affecting breast cancer risk. Maturitas 2010;66:33-8.
41. Winzer BM, Whiteman DC, Reeves MM, et al. Physical activity and cancer prevention: a systematic review of clinical trials. Cancer Causes Control 2011;22:811-26.
42. Physical Activity and Cancer. 2017. Available online: https://www.cancer.gov/about-cancer/causes-prevention/risk/obesity/physical-activity-fact-sheet#r23
43. Bondurant KL, Harvey S, Klimberg S, et al. Establishment of a southern breast cancer cohort. Breast J 2011;17:281-8.
44. Lee JY, Klimberg S, Bondurant KL, et al. Cross-sectional study to assess the association of population density with predicted breast cancer risk. Breast J 2014;20:615-21.
45. Arkansas Cancer Registry. Health ADo.
46. Lee IM, Paffenbarger RS Jr. Associations of light, moderate, and vigorous intensity physical activity with longevity. The Harvard Alumni Health Study. Am J Epidemiol 2000;151:293-9.
47. Duvivier BM, Schaper NC, Bremers MA, et al. Minimal intensity physical activity (standing and walking) of longer duration improves insulin action and plasma lipids more than shorter periods of moderate to vigorous exercise (cycling) in sedentary subjects when energy expenditure is comparable. PLoS One 2013;8:e55542.
48. Measuring Physical Activity. In: The Nutrition Source. Harvard T.H.Chan School of Public Health. Available online: https://www.hsph.harvard.edu/nutritionsource/mets-activity-table/
49. Ainsworth BE, Haskell WL, Herrmann SD, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. Med Sci Sports Exerc 2011;43:1575-81.
50. Jette M, Sidney K, Blumchen G. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. Clin Cardiol 1990;13:555-65.
51. Fan JX, Wen M, Kowaleski-Jones L. Rural-urban differences in objective and subjective measures of physical activity: findings from the National Health and Nutrition Examination Survey (NHANES) 2003-2006. Prev Chronic Dis 2014;11:E141.
52. Key Statistics for Breast Cancer in Men. 2019. Available online: https://www.cancer.org/cancer/breast-cancer-in-men/about/key-statistics.html
53. Mertens AJ, Sweeney C, Shahar E, et al. Physical activity and breast cancer incidence in middle-aged women: a prospective cohort study. Breast Cancer Res Treat 2006;97:209-14.
54. Rimm EB, Stampfer MJ, Colditz GA, et al. Validity of self-reported waist and hip circumferences in men and women. Epidemiology 1990;1:466-73.

**Cite this article as:** Stahr SD, Runnells GA, Rogers LJ, McElfish PA, Kadlubar SA, Su LJ. Association between breast cancer risk and leisure physical activity in a rural cohort population. Transl Cancer Res 2019;8(Suppl 4):S366-S377. doi: 10.21037/tcr.2019.06.18

 