

# The Relationship Between Sleep and Weight Change Among Women Diagnosed with Breast Cancer Participating in the Women's Health Initiative

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# Abstract

**Purpose:** Short and long sleep duration and poor sleep quality are risk factors for weight gain and cancer mortality. The purpose of this study is to investigate the relationship between sleep and weight change among postmenopausal breast cancer survivors.

**Methods:** Women participating in the Women's Health Initiative who were diagnosed with incident breast cancer between year 1 and year 3 were included. Self-reported sleep duration was categorized as  $\leq 5$  hours (short), 6 hours, 7-8 hours (optimal), and  $\geq 9$  hours (long). Self-reported sleep quality was categorized as poor, average, and above average. Post-diagnosis weight change was the difference of weight closest to, but preceding diagnosis, and year 3 weight. We used linear regression to evaluate sleep duration and sleep quality associations with post-diagnosis weight change adjusted for potential confounders.

**Results:** Among 1,156 participants, 63% were weight stable after diagnosis; average weight gain post cancer diagnosis was 3.2 kg. Six percent of women reported sleeping  $\leq 5$  hours, 26% reported 6 hours, 64% reported 7-8 hours, and 4% reported  $\geq 9$  hours. There were no differences in adjusted estimates of weight change among participants with short duration (0.37kg; 95%CI -0.88, 1.63), or long duration (-0.56kg; 95% CI -2.03, 0.90) compared to optimal duration, nor was there a difference among poor quality (-0.51kg; 95% CI -1.42, 0.41) compared to above average quality.

**Conclusion:** Among postmenopausal breast cancer survivors, sleep duration and quality were not associated with weight change after breast cancer diagnosis. Future studies should consider capturing change in adiposity and to expand beyond self-reported sleep.

## Introduction/ Background

Increased body weight and obesity are associated with heightened risk of several types of cancers, including breast cancer [1]. These factors, in addition to post-diagnosis weight gain, are also associated with elevated risk of cancer related mortality [1, 2]. Many laboratory and epidemiological studies identify sleep disturbances, including poor sleep quality, short (i.e., <6 hours), and long (i.e., >9 hours) sleep duration, as risk factors for weight gain and obesity [3]. Several biological and behavioral mechanisms and factors underlie these associations including decreased levels of leptin [4], increased levels of ghrelin [4], increased calorie consumption [5], poor diet quality [5], and decreased energy expenditure [6]. Decreased sleep duration and poor sleep quality are common among postmenopausal women [7]. A U-shaped relationship between sleep duration and body mass index (BMI) has been observed among postmenopausal women, with higher BMI among women with reported sleep duration of  $\leq 6$  hours or  $\geq 9$  hours, compared to those with 7-8 hours of sleep [8].

Menopause, breast cancer diagnosis, and related treatment effects of breast cancer each present physiological and psychological challenges that may impact short- and long-term sleep patterns in women. Menopause is a time when breast cancer risk increases and obesity becomes a risk factor for

breast cancer [9]. More specifically, obesity has been associated with an increased breast cancer risk after menopause [10]. Breast cancer survivors often report changes in sleep habits before, during, and after treatment, commonly related to vasomotor symptoms such as hot flashes, [11] making this population particularly vulnerable to sleep-related weight change.

There has been limited research to date examining the relationship between sleep quality, sleep duration and body weight change among postmenopausal breast cancer survivors. Previous research has shown that poorer sleep quality and shorter sleep duration are more commonly observed in postmenopausal breast cancer survivors as compared to age-matched healthy, postmenopausal women [12, 13]. In one study, postmenopausal breast cancer survivors who reported any (temporary or sustained) change in sleep duration at the 30-month follow-up time point were 1.82 times more likely to have gained <sup>3</sup>5% of baseline body weight compared to women who reported no change in sleep duration [11]. However, we are not aware of any study that has examined the relationship between sleep and weight change specifically in postmenopausal breast cancer survivors. Understanding the relationship between sleep and weight change in this population is worthwhile because sleep habits are modifiable and may be an important aspect of weight loss interventions aimed to improve breast cancer prognosis.

The rich data available from the Women's Health Initiative (WHI) provide an opportunity to evaluate sleep and its association with subsequent weight change in postmenopausal women after a diagnosis of breast cancer, in addition to an extensive collection of measures which may confound this relationship. The objectives of our analyses are to: (1) describe pre-cancer diagnosis (baseline) sleep duration, sleep quality, and weight change in women diagnosed with breast cancer between WHI study year one and year three and (2) evaluate pre-diagnosis sleep duration and sleep quality at baseline and its relationship with post-diagnosis weight change in women diagnosed with breast cancer between year one and year three. We hypothesize that women who report short sleep, long sleep, and poor sleep quality will demonstrate greater gains in body weight pre- and post-diagnosis compared to women with a sleep duration of 7-8 hours and above average sleep quality.

## **Methods And Procedures**

### ***Study Design***

This was a secondary analysis using data from the WHI. The WHI is a longitudinal study investigating healthy aging among more than 161,000 postmenopausal women. The WHI began in 1993 with 40 clinical centers nationwide and recruited women aged 50-79 years into either one or more of three randomized clinical trials (CT) or an observational study (OS)[14]. The design and selection criteria of the WHI has been described previously [15]. Data were collected at routine clinical examinations and using questionnaires. Institutional Review Boards at all participating WHI institutions approved the study protocols and all participants provided informed consent prior to study participation.

## ***Inclusion / Exclusion Criteria***

From the WHI CT and OS, we included women who developed breast cancer between year 1 and year 3, had sleep duration and sleep quality reported at baseline, and had weight collected at baseline, pre-diagnosis, and year 3. We then excluded women who had a personal history of breast cancer before baseline or were missing data for the covariates, with the exception of income for which we created an indicator variable for missing income.

Breast cancer diagnosis was collected via questionnaires mailed to participants every six months. Women who did not send in the completed questionnaire were contacted by trained study outcomes coordinators to complete the information by telephone. If women were not able to complete the questionnaire, proxy contacts, provided by the participants, were reached to collect the information. All reported breast cancer diagnoses were adjudicated by centrally trained physicians using medical records including cancer pathology reports [16]. Between years one and three, 1,595 WHI participants were diagnosed with breast cancer.

## ***Exposures of Interest***

**Sleep Duration:** Baseline sleep duration was collected via the self-report WHI Lifestyle Questionnaire according to the question: “About how many hours of sleep did you get on a typical night during the past 4 weeks?”, with possible responses of:  $\leq 5$  hours, 6 hours, 7 hours, 8 hours, 9 hours, and  $\geq 10$  hours. To be consistent with previous WHI studies [17, 18], we collapsed these categories into four levels: short sleep (5 or less hours), 6 hours, long sleep (9 hours or more) [19] and the reference group of optimal sleep (7 or 8 hours)[19, 20].

**Sleep Quality:** Baseline sleep quality was collected via the self-report WHI Lifestyle Questionnaire and was assessed using the question: “Overall, was your typical night's sleep during the past 4 weeks”, with possible responses of: “very sound or restful, sound or restful, average quality, restless, or very restless?”. We collapsed these categories into three levels: poor sleep quality (“very restless” or “restless”), average sleep quality (average quality) and the reference group of above average sleep quality (very sound or restful).

## ***Primary Outcome***

Clinical examinations were completed for participants at routine study clinic visits according to corresponding study arm schedule to collect weight (kg). All women attending the clinic visit completed a measurement of height and body weight, following a standardized WHI protocol, using a beam scale, with height recorded to the nearest 0.1 centimeter and weight recorded to the nearest 0.1 kilogram. All weights were assessed by trained clinic staff. Weight change in kilograms (kg) was calculated as the change in weight from baseline to year 3 and pre-diagnosis to year three. Pre-diagnosis weight was the

weight recorded closest to but preceding diagnosis. For participants of the OS, weight was collected at baseline and year 3, and for CT participants, weight was collected at baseline, year 1, 2, and 3. Thus, weight change from baseline to year 3 and pre-diagnosis to year 3 was the same for participants of the OS.

*A priori* power calculations showed that a weight change of 7kg, 2kg, and 5kg would be detected for the  $\leq 5$  hours, 6 hours, and  $\geq 9$  hours sleep duration group at 80% power when compared to the 7-8 hour sleep duration group. Compared to the above average sleep quality group, a weight change of 4kg would be detected for the poor sleep group and a weight change of 3kg would be detected for the average sleep quality group at 80% power.

## ***Covariates***

Baseline covariates were derived from the literature and include age, race/ethnicity, marital status, education, employment status, family income, BMI, smoking status, alcohol consumption, caffeine consumption, total physical activity in metabolic equivalent (MET) -hours/week, dietary energy (kcal/day), pain construct score, depression construct score, prevalent diabetes, prevalent arthritis, prevalent hypertension, use of sleep medication, and breast cancer factors (cancer stage at diagnosis, years from baseline to diagnosis), use of HRT at baseline, and use of anti-neoplastic hormonal medications post-diagnosis [21-23]. Additionally, participation in the hormone replacement therapy (HRT), dietary modification (DM), or calcium and vitamin D (CaD) intervention was controlled for because women who were eligible for these clinical trials were on average healthier than those who were in the observational study, and because the interventions may have impacted weight and/or sleep. Self-reported race and ethnicity of American Indian or Alaskan Native, Asian or Pacific Islander, Hispanic/Latino, and other were aggregated due to small sample sizes to create a single category. Self-reported race and ethnicity of white and black or African American were also reported.

## **Statistical Methods**

Descriptive statistics at baseline were stratified by sleep duration ( $\leq 5$  hours, 6 hours, 7-8 hours,  $\geq 9$  hours). The relationship between baseline sleep duration and sleep quality with weight change was described using mean and 95% confidence interval (CI) and plotted for visual description.

We used linear regression to evaluate the relationship between sleep duration at baseline and weight change, as well as sleep quality at baseline and weight change. We fit both unadjusted and adjusted models adjusting for age, race/ethnicity, marital status, education, employment status, family income, BMI, smoking status, alcohol consumption, caffeine consumption, total physical activity in metabolic equivalent (MET)-hours/week, dietary energy (kcal/day), pain construct score, depression construct score, prevalent diabetes, prevalent arthritis, prevalent hypertension, use of sleep medication, and breast

cancer factors (cancer stage at diagnosis, years from baseline to diagnosis), study arm, use of HRT at baseline, and use of anti-neoplastic hormonal medications post-diagnosis.

We performed sensitivity analyses to examine the potential influence of the WHI study arm on weight change. In this analysis, women who participated in the DM study arm were removed, but the analyses were otherwise identical to the primary adjusted and unadjusted models.

All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC, USA), tests were two-sided with a specified type I error rate of  $\alpha = 0.05$ .

## Results

### *Participant Characteristics*

A total of 1,173 WHI study participants who were diagnosed with incident breast cancer between years one and three were included in the analysis. Baseline characteristics are reported in Table 1. Overall, 6.2% of women slept 5 hours or less, 25.7% slept 6 hours, 64.1% slept 7-8 hours, and 4.0% slept 9 hours or more. Women who slept less had higher BMI, lower physical activity rates, and greater prevalence of comorbid conditions. Use of sleep medication was prevalent in 21.7% of the sample and proportions were not significantly different between groups. Additionally, 48.4% of women had any weight gain in the one to three years post breast cancer diagnosis with a mean weight gain of 3.2 kg ( $\pm 3.0$ ).

**Table 1**

Baseline characteristics of women participating in the WHI who developed breast cancer between year 1 and year 3 of study, stratified by self-reported sleep duration at baseline, n=1,156

Baseline characteristics,	£ 5 hours	6 hours	7-8 hours	<sup>3</sup> 9 hours
n (%) or mean (SD)	72 (6.2)	297 (25.7)	741 (64.1)	46 (4.0)
Age, years	64.1 (7.2)	64.0 (6.9)	64.3 (6.6)	65.8 (5.9)
Race				
White	49 (68.1)	253 (85.2)	670 (90.4)	43 (93.5)
Black or African American	14 (19.4)	24 (8.1)	27 (3.6)	2 (4.3)
American Indian or Alaskan native, Asian or Pacific Islander, Hispanic/Latino, or other*	9 (12.5)	20 (6.7)	44 (5.9)	1 (2.2)
Marital status				
Married / living as married	38 (52.8)	186 (62.6)	505 (68.2)	32 (69.6)
Divorced / living separate	22 (30.6)	70 (23.6)	122 (16.5)	9 (19.6)
Widowed	12 (16.7)	41 (13.8)	126 (17.0)	7 (15.2)
Education level				
High School or less	15 (20.8)	56 (18.9)	126 (17.0)	7 (15.2)
Some college / Associate's degree / trade school	36 (50.0)	114 (38.4)	256 (34.5)	20 (43.5)
College graduate or greater	21 (29.2)	127 (42.8)	359 (48.4)	19 (41.3)
Employment status <sup>a</sup>				
Employed	18 (25.0)	135 (45.5)	229 (30.9)	11 (23.9)
Retired	10 (13.9)	24 (8.1)	71 (9.6)	3 (6.5)
Homemaker	36 (50.0)	146 (49.2)	409 (55.2)	32 (69.6)
Not working / other	8 (11.1)	21 (7.1)	61 (8.2)	4 (8.7)
Family income				
< \$20,000	16	36	82	5 (10.9)

	(22.2)	(12.1)	(11.1)	
\$20,000 to \$49,999	41 (56.9)	140 (47.1)	296 (39.9)	23 (50.0)
<sup>3</sup> \$50,000	12 (16.7)	112 (37.7)	323 (43.6)	14 (30.4)
Missing or unknown	3 (4.2)	9 (3.0)	40 (5.4)	4 (8.7)
Smoking status				
Never	38 (52.8)	144 (48.5)	370 (49.9)	21 (45.7)
Former	28 (38.9)	139 (46.8)	338 (45.6)	22 (47.8)
Current	6 (8.3)	14 (4.7)	33 (4.5)	3 (6.5)
Alcohol consumption, drinks/wk				
Non-drinker	5 (6.9)	22 (7.4)	56 (7.6)	5 (10.9)
Past-drinker	19 (26.4)	53 (17.8)	109 (14.7)	7 (15.2)
< 7	40 (55.6)	178 (59.9)	463 (62.5)	23 (50.0)
<sup>3</sup> 7	8 (11.1)	44 (14.8)	113 (15.2)	11 (23.9)
Coffee consumption, cups/day				
< 1	35 (48.6)	129 (43.4)	308 (41.6)	15 (32.6)
1-2	25 (34.7)	113 (38.0)	272 (36.7)	18 (39.1)
<sup>3</sup> 3	12 (16.7)	55 (18.5)	161 (21.7)	13 (28.3)
Physical activity, MET hr/wk				
	12.4 (14.7)	13.6 (16.4)	13.4 (13.6)	11.9 (12.1)
Dietary energy, kcal/day				
	1,719.6 (686.4)	1,691.1 (741.6)	1,672.0 (624.1)	1,586.7 (611.9)
Pain, construct score <sup>b</sup>				
	65.1 (25.9)	75.3 (21.3)	77.1 (21.3)	79.9 (16.6)
Depression, construct score <sup>c</sup>				
	0.10 (0.21)	0.05 (0.13)	0.02 (0.07)	0.01 (0.03)
Weight, kg				
	75.3 (17.5)	74.5 (15.1)	72.4 (14.5)	68.6 (11.0)

BMI, kg/m <sup>2</sup>				
Underweight or normal weight (< 24.9)	26 (36.1)	85 (28.6)	293 (39.5)	19 (41.3)
Overweight (25.0-29.9)	16 (22.2)	106 (35.7)	248 (33.5)	20 (43.5)
Obese (≥30.0)	30 (41.7)	106 (35.7)	200 (27.0)	7 (15.2)
Cancer stage				
In situ	16 (22.2)	63 (21.2)	146 (19.7)	10 (21.7)
Localized	36 (50.0)	166 (55.9)	454 (61.3)	32 (69.6)
Regional	19 (26.4)	62 (20.9)	127 (17.1)	4 (8.7)
Distant / unknown	1 (1.4)	6 (2.0)	14 (1.9)	0 (0.0)
Baseline to diagnosis time, years	2.0 (0.6)	2.0 (0.6)	2.0 (0.6)	2.0 (0.6)
Prevalent hypertension	33 (45.8)	106 (35.7)	242 (32.7)	19 (41.3)
Prevalent diabetes	8 (11.1)	16 (5.4)	33 (4.5)	2 (4.3)
Prevalent arthritis	46 (63.9)	144 (48.5)	333 (44.9)	21 (45.7)
Use of sleep medication, use/week				
Not in the past 4 weeks	53 (73.6)	230 (77.4)	587 (79.2)	35 (76.1)
≤ 2	9 (12.5)	39 (13.1)	81 (10.9)	3 (6.5)
3-4	5 (6.9)	8 (2.7)	15 (2.0)	0 (0.0)
≥ 4	6 (8.3)	14 (4.7)	34 (4.6)	3 (6.5)
Use of estrogen ± progesterone pre-diagnosis	38 (52.8)	206 (69.4)	501 (67.6)	31 (67.4)
Use of anti-neoplastic hormonal medications post-diagnosis <sup>d</sup>	40 (55.6)	217 (73.1)	552 (74.5)	33 (71.7)
Age at menopause, years	47.7 (7.1)	49.2 (6.2)	49.1 (5.9)	48.6 (6.5)
Trial Arm <sup>e</sup>				
OS	33	175	432	31

	(45.8)	(58.9)	(58.3)	(67.4)
HRT intervention	13 (18.1)	40 (13.5)	88 (11.9)	5 (10.9)
DM intervention	29 (40.3)	96 (32.3)	256 (34.5)	11 (23.9)
CaD intervention	15 (20.8)	68 (22.9)	160 (21.6)	8 (17.4)

Abbreviations: WHI, Women's Health Initiative; BMI, body mass index; MET, metabolic equivalent; OS, observational study; HRT, hormone replacement therapy; DM, dietary modification; CaD, calcium and vitamin D

\* Individual self-reported race/ethnicity distribution is as follows: American Indian or Alaskan Native, n=3; Asian or Pacific Islander, n=30; Hispanic/Latino, n=30; other race, n=11

<sup>a</sup> Employment status levels are not mutually exclusive as participants could have selected more than one option

<sup>b</sup> Measured using the pain subscale of the Rand-36 Item Health Survey with potential scores ranging from 0-100 where higher scores index more favorable health status

<sup>c</sup> Measured using the Center for Epidemiological Studies Depression Scale (CES-D) with potential scores ranging from 0-1 where higher scores indicate greater likelihood of depression

<sup>d</sup> Anti-neoplastic hormonal medications post-diagnosis include selective estrogen receptor modulators and aromatase inhibitors

<sup>e</sup> Not mutually exclusive, as participants could have been in one or multiple trials

## ***Primary Analysis***

The relationship between baseline sleep duration and sleep quality with weight at the three time intervals (baseline, pre-diagnosis, and year three) (panel a) and weight change between baseline and year three was plotted (Figure 2). The mean weight for participants with short sleep duration at all time points was higher than the other sleep duration categories, but this difference was not significant. On average, women who slept 5 hours or less had non-statistically significant weight increase from baseline to year three (0.28 kg; 95% CI -0.88, 1.44) and from pre-diagnosis to year 3 (0.37 kg; 95% CI -0.60, 1.33). For participants with long sleep duration, poor sleep quality, and above average sleep quality, weight decreased from baseline to year three while all other categories had non-statistically significant weight change. Point estimates for all categories indicated weight loss from pre-diagnosis to year three with the exception of short sleep, however all changes were not statistically significant.

In unadjusted and adjusted models (Table 2), women who slept  $\leq$  5 hours (adjusted weight change estimate: 0.37kg; 95% CI -0.88, 1.63) or  $\geq$  9 hours (adjusted weight change estimate: -0.56kg; 95% CI -2.03,

0.90) did not have meaningful change in weight compared to those who slept 7-8 hours. We observed no difference in weight gain among women reporting poor sleep (adjusted weight change estimate: -0.51kg; 95% CI -1.42, 0.41) nor average sleep quality (adjusted weight change estimate: 0.13kg; 95% CI -0.50, 0.76) when compared to the above average sleep quality group (Table 2).

**Table 2**

Linear regression results for the association between sleep duration and sleep quality at baseline and weight change from pre-diagnosis to year 3, n=1,156

	Crude Model		Adjusted Model <sup>a</sup>	
	Estimated weight change, kg	95% CI	Estimated weight change, kg	95% CI
<b>Sleep duration</b>				
£ 5 hours	0.74	-0.46, 1.94	0.37	-0.88, 1.63
6 hours	-0.17	-0.84, 0.50	-0.19	-0.86, 0.48
7-8 hours	ref		ref	
<sup>3</sup> 9 hours	-0.53	-2.01, 0.95	-0.56	-2.03, 0.90
<b>Sleep quality</b>				
Poor quality	-0.38	-1.24, 0.49	-0.51	-1.42, 0.41
Average quality	0.09	-0.53, 0.71	0.13	-0.50, 0.76
Above average quality	ref		ref	

<sup>a</sup> Adjusted for age, race, marital status, education, employment status, family income, smoking status, alcohol consumption, caffeine consumption, BMI, total physical activity, dietary energy, pain, depression, cancer stage, years from baseline to diagnosis, prevalent diabetes, prevalent arthritis, prevalent hypertension, use of sleep medication, use of HRT pre-diagnosis, use of anti-neoplastic hormonal medications post-diagnosis, and study arm

After removing participants in the DM study arm for a sensitivity analysis, results were similar to those of the primary adjusted models. We observed no difference in weight gain among women reporting short sleep (adjusted weight change estimate: 0.37kg; 95% CI -1.22, 1.96) or poor sleep quality (adjusted weight change estimate: -0.19kg; 95% CI -1.34, 0.96) when compared to the respective referent group.

**Table 3**

Sensitivity results for the association between sleep duration and sleep quality at baseline and weight change from pre-diagnosis to year 3 excluding DM intervention participants, n=764

	Crude Model		Adjusted Model <sup>a</sup>	
	Estimated weight change, kg	95% CI	Estimated weight change, kg	95% CI
Sleep duration				
£ 5 hours	0.93	-0.62, 2.48	0.37	-1.22, 1.96
6 hours	-0.30	-1.14, 0.54	-0.45	-1.30, 0.39
7-8 hours	ref		ref	
<sup>3</sup> 9 hours	-0.79	-2.55, 0.97	-0.88	-2.63, 0.88
Sleep quality				
Poor quality	0.04	-1.04, 1.13	-0.19	-1.34, 0.96
Average quality	0.16	-0.62, 0.95	0.18	-0.63, 0.99
Above average quality	ref		ref	

Abbreviations: WHI, Women’s Health Initiative; DM, dietary modification

<sup>a</sup> Adjusted for age, race, marital status, education, employment status, family income, smoking status, alcohol consumption, caffeine consumption, BMI, total physical activity, dietary energy, pain, depression, cancer stage, years from baseline to diagnosis, prevalent diabetes, prevalent arthritis, prevalent hypertension, use of sleep medication, use of HRT pre-diagnosis, use of anti-neoplastic hormonal medications post-diagnosis, and study arm.

## Discussion

In this large study of postmenopausal breast cancer survivors, we hypothesized that there would be a positive association between short sleep, long sleep, and poor sleep quality with post cancer diagnosis weight gain. However, no significant associations were observed between short sleep, long sleep, and poor sleep quality and post-diagnosis weight gain in adjusted models. Cross-sectional weight at baseline, year one, and year three were trending higher, although non-significantly, in women who reported shorter

sleep duration, but surprisingly, cross-sectional weight appeared similar according to sleep quality (Figure 2).

We propose several possible explanations for our unexpected null findings. First, the distribution of weight change after breast cancer diagnosis in our sample was inconsistent compared to prior studies [24-28]. In our sample 64.4% of women were weight stable ( $\pm 5\%$  of body weight), 16.7% gained more than 5% of body weight and 18.9% lost more than 5% of body weight. We suspected that participation in the DM study may have been a contributing factor to the relatively stable distribution of weight change, yet adjusting for DM intervention participation and even excluding these participants in a sensitivity analysis did not appreciably change these results (Table 3). Our findings build on previous evidence from the WHI, where there was similar distribution of weight change among women in the OS cohort to our sample of breast cancer survivors [29]. Prior reports found weight gain frequencies of 40-70% after a breast cancer diagnosis [24-27], with greater weight gain seen among postmenopausal women [24-26], those diagnosed with advanced stage breast cancer [25], and those who received chemotherapy [24, 26, 28]. In our study, results from post-hoc analyses showed no differences in post-diagnosis weight change were seen among early and advanced stage diagnoses. However, 80.0% of our sample was considered early stage, owing to the expectation of regular mammogram screening during trial participation [30]. Finally, we considered that changes in sleep duration and quality after breast cancer diagnosis might have impacted our results. However, we do not think this explains our results because sleep duration and quality were stable for a majority of the participants; 66% of our sample remained stable in reported sleep duration and 59.0% stable for sleep quality over time. In addition, post-hoc analyses using later (year three) measures of sleep (adjusted for baseline sleep) revealed no association between weight change and sleep duration or sleep quality (results not shown).

We completed several additional post-hoc analyses to attempt to explain our findings. We examined the possibility of physical activity and dietary energy being effect modifiers, but found no indication of interaction when using a threshold of  $p \leq 0.2$ . We additionally adjusted for age at menopause which did not meaningfully change results. Lastly, we included the 141 participants who were excluded due to missing covariates and removed those covariates from the multivariate model and found no association.

To our knowledge, no previous study has examined the association of sleep duration and sleep quality with weight change among postmenopausal breast cancer survivors. Previous studies have found that this population is particularly susceptible to experiencing short- and long-term changes in sleep habits after diagnosis [12, 31], however, this is counter to our findings on long-term sleep changes as the majority of our population remained stable in sleep duration and quality from baseline to year 3 follow-up, an average 24 months post-diagnosis. While not breast cancer specific, Patel et al. [21] examined the association of sleep duration with weight change among women aged 39-65 years and free of comorbidities who were participating in the Nurses' Health Study. Statistically significant mean weight gain differences among women who reported sleeping  $\leq 5$  hours and 6 hours as compared to those sleeping 7 hours over 4, 8, 12, and 16 years of follow-up were found.

Current literature regarding the relationship of long sleep and weight are mixed, as some studies have observed a U-shaped relationship [8, 32, 33] and others an inverse relationship [3, 21, 34, 35]. It has been proposed that long sleep duration (generally <sup>3</sup> 9 hours) is associated with increased weight and BMI as long sleepers may engage in less physical activity [36]. Our study showed no association between cross-sectional weight or weight gain and long sleep as hypothesized. Baseline self-reported physical activity was the lowest among long sleepers, however, long sleepers reported lower energy intake and had the lowest weight point estimates at baseline, pre-diagnosis, and year three when compared to the other sleep duration groups.

Strengths of this analysis include the WHI's large sample and prospective design with robust follow-up of study participants. Detailed information was available related to potential confounders and variables that were collected through standardized data collection protocols and validated instruments. Cancer outcomes were adjudicated and weight measurements were completed in clinic by trained staff, thereby reducing risk of reporting bias.

There were several limitations that should be recognized. Although the sleep questions were developed by sleep researchers consulting to the WHI Behavioral Advisory Committee [37], sleep duration and sleep quality were each collected using a single question rather than an extensive, validated questionnaire. Additionally, we did not have data on the type of cancer treatment received, which could potentially influence both sleep and weight change, particularly with chemotherapy related side-effects being associated with sleep disturbances [38-41] and adjuvant chemotherapy leading to greater weight gain compared to patients who did not receive chemotherapy [26]. We did, however, adjust for cancer stage, which is associated with treatment type, and may act as a reasonable proxy. We suspect the cohort effects may play a role [42]; these data were collected from 1993-2005, before substantial increases in sedentary time, TV watching, and screen time [43], and decreases in sleep duration among adults in the US [44, 45]. These changes in health behaviors in the last three decades, may not represent current sleep and weight trends. Further, we did not analyze long-term weight change beyond year three follow-up which may or may not have similar trends. For some OS participants weight at baseline may have been used for pre-diagnosis weight as weight measured at year 1 was not collected for these women, only being collected for the participants participating in the CT. Lastly, although the race and ethnicity distribution of the WHI study population was fairly similar to that reported by the US census from 1993 to 1998, the demographic of older-aged women in the US has since become more diverse [46]. Thus, the study sample and related results may not reflect the current race and ethnic distribution of postmenopausal women in the US. While the WHI is a large cohort of postmenopausal women, the sample size of breast cancer survivors was limited. There remains a need for larger studies with diverse samples of breast cancer survivors in future research.

In conclusion, sleep duration and sleep quality were not found to be associated with weight change after breast cancer diagnosis among postmenopausal breast cancer survivors participating in the WHI. Both weight and sleep were stable after breast cancer diagnosis. Replication in other more recent samples that include more variance in stage at diagnosis and treatment type, as well as more rigorous sleep and

adiposity measures, would afford a more robust analysis of sleep and weight patterns commonly reported among postmenopausal breast cancer survivors.

## **Declarations**

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### **Conflicts of Interest:**

Authors have reported no conflicts of interest.

### **Availability of data and material:**

The data used was from the Women's Health Initiative.

### **Code Availability:**

SAS 9.4 (SAS Institute, Cary, NC, USA)

### **Ethics approval:**

Institutional Review Boards at all participating WHI institutions approved the study protocols and all participants provided informed consent prior to study participation.

### **Consent to participate:**

Institutional Review Boards at all participating WHI institutions approved the study protocols and all participants provided informed consent prior to study participation.

### **Consent to publication:**

The WHI review board has approved this manuscript (MS4305) for publication.

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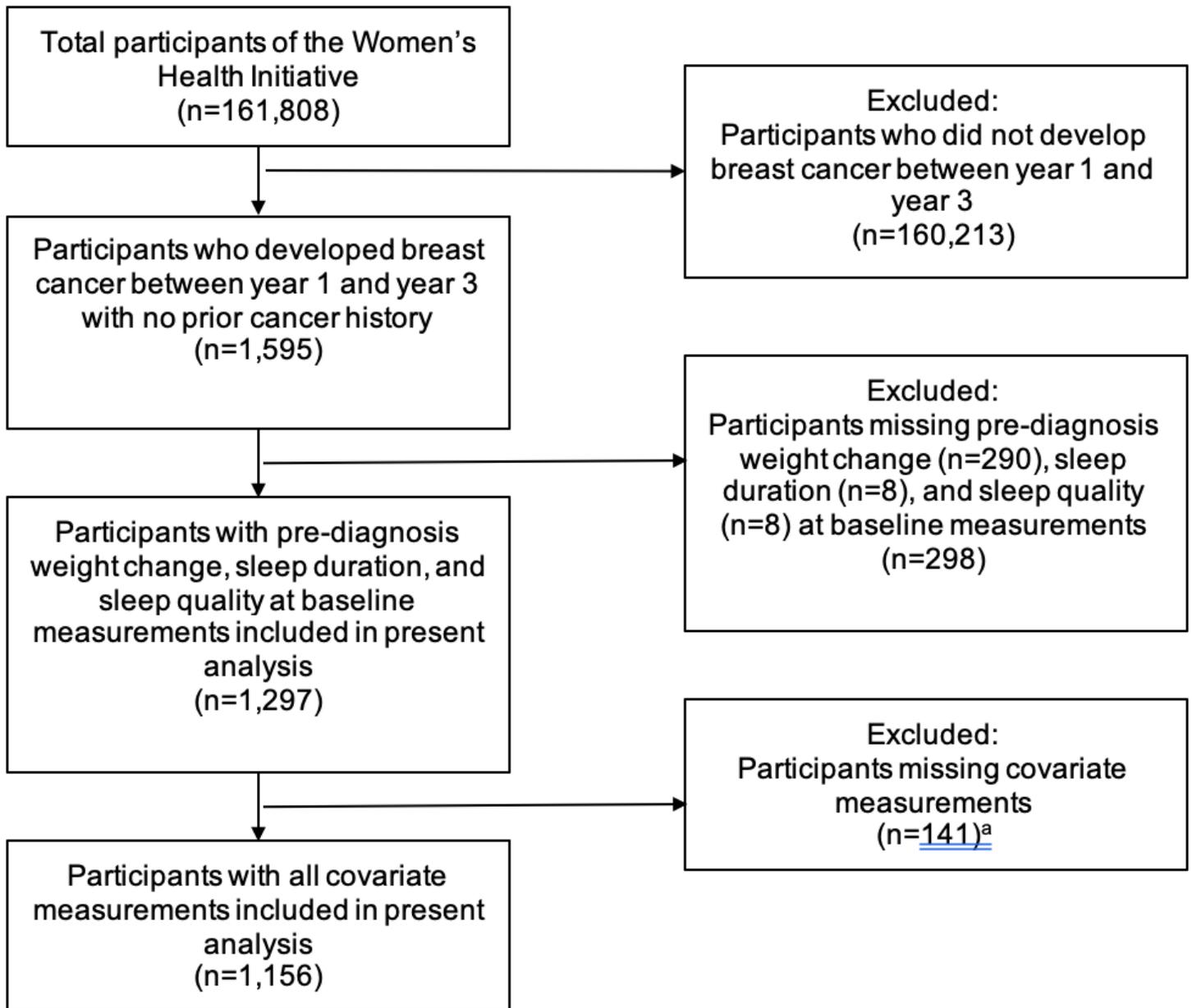
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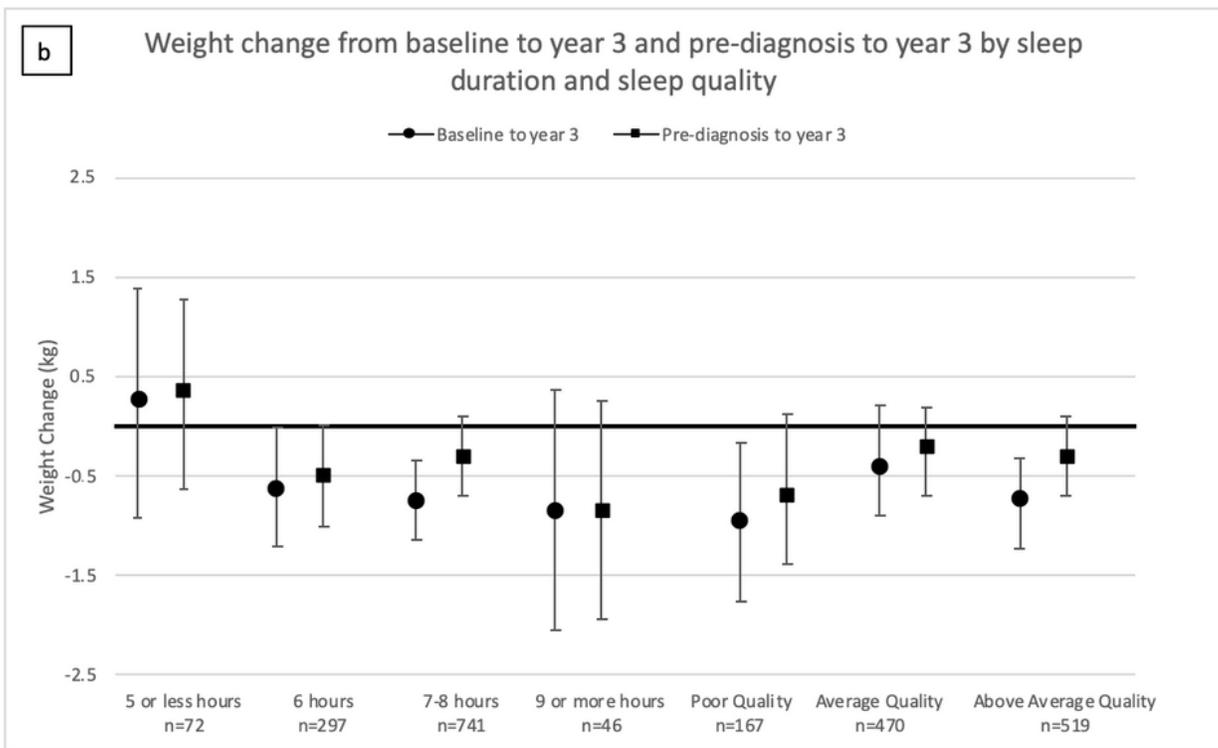
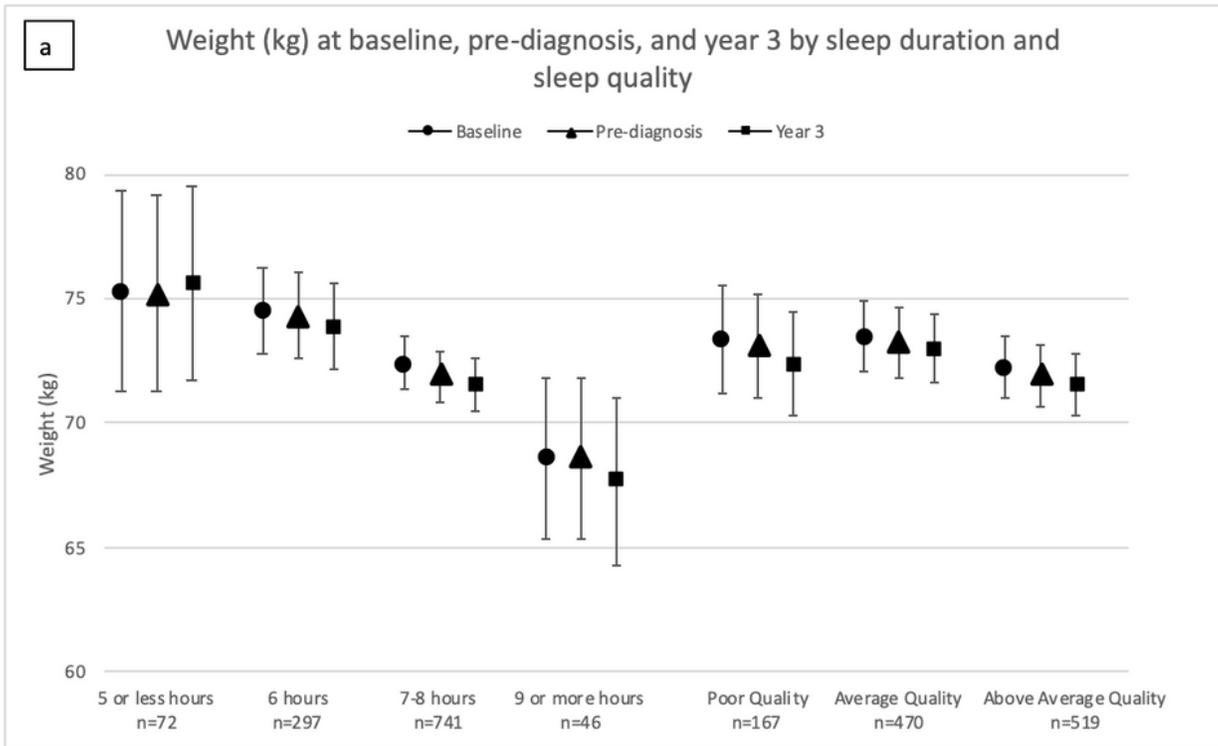
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## Figures



**Figure 1**

Figure 1. Sample size and exclusions a Distribution of missing covariates may overlap and include: use of sleep medicine, n=3; prevalent arthritis, n=13; prevalent hypertension, n=3; smoking status, n=16; education level, n=11; race/ethnicity, n=3; BMI, n=3; marital status, n=9; physical activity, n=53; dietary energy, n=3; pain, n=6; depression, n=38



**Figure 2**

Average weight (a), average weight change (b), and 95% CI by self-reported sleep duration and sleep quality, among WHI women diagnosed with breast cancer between year 1-3 of study, n=1,156  
 Abbreviations: WHI, Women's Health Initiative