UC Irvine
UC Irvine Previously Published Works

Title

Frequency of Consuming Breakfast Meals and After-Dinner Snacks Is not Associated with Postmenopausal Breast Cancer Risk: Womens Health Initiative Observational Study.

Permalink

https://escholarship.org/uc/item/9qr306pt

Journal

The Journal of Nutrition, 153(4)

Authors

Elahy, Valeria

Thomson, Cynthia

Neuhouser, Marian

et al.

Publication Date

2023-04-01

DOI

10.1016/j.tjnut.2023.02.003

Peer reviewed

eScholarship.org Powered by the California Digital Library
University of California

The Journal of Nutrition 153 (2023) 1089–1100

American Society for Nutrition
Excellence in Nutrition Research and Practice

JN THE JOURNAL OF NUTRITION

journal homepage: www.journals.elsevier.com/the-journal-of-nutrition

Nutritional Epidemiology

Frequency of Consuming Breakfast Meals and After-Dinner Snacks Is not Associated with Postmenopausal Breast Cancer Risk: Women's Health Initiative Observational Study

Valeria Elahy [1], Cynthia Thomson [2], Marian L. Neuhouser [3], Luohua Jiang [1], Sunmin Lee [8], Kathy Pan [4], Mara Vitolins [5], Rowan Chlebowski [6], Dorothy Lane [7], Andrew O. Odegaard [1,*]

[1] *Department of Epidemiology and Biostatistics, University of California, Irvine, CA, USA;* [2] *Department of Health Promotion Sciences, University of Arizona, Tucson, AZ, USA;* [3] *Cancer Prevention Program, Fred Hutchinson Cancer Center, Seattle, WA, USA;* [4] *Department of Hematology/ Oncology, Kaiser Permanente Southern California, Downey, CA, USA;* [5] *Department of Epidemiology and Prevention, Wake Forest University School of Medicine, Winston-Salem, NC, USA;* [6] *Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center, Torrance, CA, USA;* [7] *Department of Family, Population and Preventive Medicine, Renaissance School of Medicine at Stony Brook University, Stony Brook, NY, USA;* [8] *Department of Medicine, School of Medicine, University of California, Irvine, CA, USA*

A B S T R A C T

Background: There has been little investigation into how the timing of meals and eating occasions associates with postmenopausal breast cancer risk.

Objective: We examined the association between the frequency of consuming breakfast meals and after-dinner snacks with the risk for postmenopausal breast cancer.

Methods: A prospective analysis of 74,825 postmenopausal women aged 49 to 81 y from the Women's Health Initiative Observational Study cohort. Breakfast and after-dinner snack intake were assessed at year 1 examination. Risk for invasive and in situ breast cancer diagnosed before 28 February 2020 was modeled with multivariable Cox proportional hazards regression models according to breakfast and after-dinner snack consumption frequencies. The models were adjusted for age, self-identified race/ethnicity, education, income, physical activity, smoking, alcohol intake, diet quality score (Healthy Eating Index 2015), energy intake, diabetic status, hormone therapy, and BMI.

Results: During the follow-up period, 5313 participants were diagnosed with invasive breast cancer and 1197 participants with in situ breast cancer. Compared with participants who did not eat breakfast, those with daily breakfast consumption was not associated with invasive breast cancer (HR: 1.04; 95% CI: 0.9, 1.19) nor in situ (HR: 1.25; 95% CI: 0.91, 1.74) breast cancer. There were monotonic higher point estimates of in situ breast cancer for each higher category of breakfast intake from 0 to 7 times per week (P-trend = 0.04, Wald test). Compared with consumption of daily after-dinner snacks, avoidance of after-dinner snacks was not associated with invasive breast cancer (HR: 0.97; 95% CI: 0.87, 1.08) nor in situ (HR: 1.12; 95% CI: 0.89, 1.42) breast cancer.

Conclusions: There was no association between intake frequency of breakfast meals or after-dinner snack habits and with risk of breast cancer in postmenopausal women.

Keywords: breakfast, after-dinner snack, meal timing, circadian rhythm, cancer, breast cancer

Introduction

There is evidence that disruptions to circadian rhythms in humans are associated with the development of several cancer types, including breast cancer [1]. Consumption of breakfast and after-dinner snacks directly affects the length of the night fast, altering the circadian rhythms [2]. A study has shown that skipping breakfast affects circadian clocks independently from the sleep–wake cycle [3]. On the molecular level, disruption of melatonin and cortisol synthesis and associated signaling pathways affects normal breast epithelium and activates breast cancer cell growth [4,5]. In addition, breakfast consumption is associated with a greater plasma melatonin concentration [6], and late-night food consumption has been associated with

Abbreviations used: ER, estrogen receptor; HEI, Healthy Eating Index; PR, progesterone receptor; WHI OS, Women's Health Initiative Observational Study.

* Corresponding author. *E-mail address:* aodegaar@hs.uci.edu (A.O. Odegaard).

https://doi.org/10.1016/j.tjnut.2023.02.003
Received 1 November 2022; Received in revised form 31 January 2023; Accepted 3 February 2023; Available online 8 February 2023
0022-3166/© 2023 American Society for Nutrition. Published by Elsevier Inc. All rights reserved.

alteration of the synthesis of plasma cortisol [7,8]. Further biological rationale for the role of the timing of eating occasions in cancer etiology is supported by a cross-sectional study that reported a 3-h longer nighttime fasting duration is associated with more favorable breast cancer risk profiles [9,10].

Thus, there is evidence that meal timing, mainly eating occasions that bookend the daily meal pattern, may influence cancer risks through hormones associated with circadian rhythms [1,8]. However, there has been little investigation into how meal patterns, particularly breakfast meals and after-dinner snacks, relate to postmenopausal breast cancer risk. We analyzed data from the Women's Health Initiative (WHI) cohort to assess how the timing of eating occasions is associated with breast cancer risk. The objective of this study was to examine the relationship between the frequency of breakfast meals and after-dinner snack consumption and the risk of breast cancer among postmenopausal women. We hypothesized that a higher frequency of breakfast meals and a lower frequency of after-dinner snack consumption was inversely associated with breast cancer risk.

Methods

Women's Health Initiative

The WHI is an ongoing multicenter clinical trial and observational study (OS) designed to address major causes of morbidity and mortality in US postmenopausal women. [11]. In brief, 161,808 women aged 50–79 were recruited between 1 September 1993 and 31 December 1998. Details of the scientific rationale, eligibility requirements, and baseline characteristics of the participants in the WHI have been published elsewhere [12,13]. The WHI OS included 93,676 women, of whom >82,928 provided information on their breakfast and evening snack habits (Figure 1). The following participants were excluded from the analysis: 4765 women with a history of breast cancer or prevalent breast cancer at year 1 examination and 693 women with a missing breast cancer history where the exposures were assessed, so the focus is on incident cases after year 1; 2645 women with implausible energy intake (≥5000 kcal/d and <600 kcal/d) were also excluded. Missing data [education, $n = 1056$; alcohol intake, $n = 807$; income, $n = 3620$; smoking, $n = 1352$; BMI (kg/m^2), $n = 1330$; physical activity, $n = 760$] were imputed. Ten imputed data sets were created through regression-based multiple imputations using the Monte Carlo Markov chain method with missing at-random assumptions (proc mi command in SAS). The following covariates were used to impute incomplete variables: age, self-identified race/ethnicity, education, income, physical activity, overall diet quality and energy intake, smoking, alcohol intake, diabetic status, BMI, and hormone therapy [14].

This yielded a sample of 74,825 women for further analysis. The mean follow-up time was 14.67 y (95% CI: 14.62, 14.72 y).

Measurement of exposure and covariates

We analyzed the sample of participants who responded to the following questions: "How many times per week do you usually eat breakfast?" and "How many times per week do you usually eat an after-dinner snack?" The following categorical response options were offered to the participants: "never or less than once," "1–2 times," "3–4 times," "5–6 times," and "7 or more times." In this analysis, we measured the exposure by the number of breakfast meals and after-dinner snacks per week (on average)

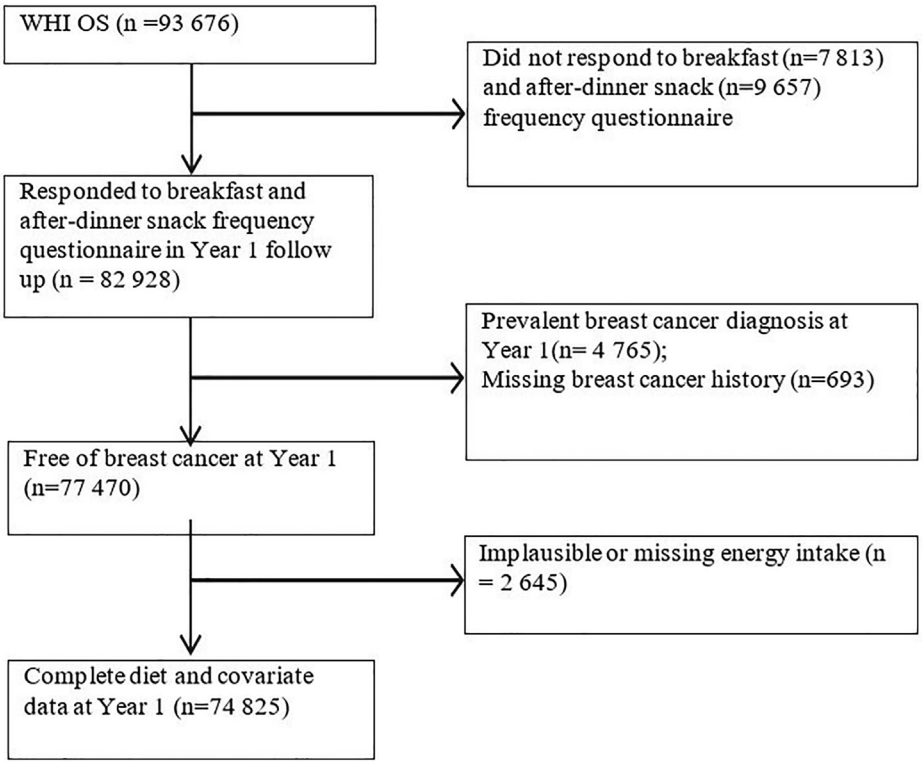

FIGURE 1. Flowchart of eligibility from the Women's Health Initiative Observational Study (WHI OS) (1994–2020).

divided into categories of 0, 1–2, 3–4, 5–6, and ≥7 times per week.

By using the observational data, we were looking for associational relative risk, which is subject to structural bias. To minimize the association due to the structural bias, we adjusted for covariates that could serve as potential confounding factors [15]. Covariates included age, self-identified race/ethnicity, education, income, physical activity, overall diet quality and energy intake, smoking, alcohol intake, diabetic status, BMI, and hormone therapy were identified as common causes of the exposure (meal frequency) and outcome (breast cancer) using directed acyclic graphs and existing evidence of the underlying confounding effect of the known covariates on the association between exposure and outcome.

In the WHI, participants self-reported demographic characteristics (age, sex, and race/ethnicity), individual socioeconomic status (education level and annual income), lifestyle behaviors (smoking status, physical activity, and alcohol intake), and medical history (hormone use, diabetic status, and mammogram screening) using self-administered standardized questionnaires during the baseline clinical visit. Overall diet quality and energy intake at the baseline were assessed using a FFQ developed and validated by the Fred Hutchinson Cancer Research Center [16]. In WHI Measurement Precision Study, questionnaire items on demographics and medical conditions were shown to be reliable (weighted $\kappa > 0.8$) [12]. Height and weight were measured at the clinic visits and used to calculate BMI as weight (kg)/height^2 (m^2). Self-reported physical activity was measured by a recreational physical activity score (metabolic equivalent tasks-hour per week) based on a series of questions related to exercise intensity levels, which has been shown to be reliable (range of weightedκ: 0.67–0.71) and valid when compared with accelerometer data ($r = 0.73$) [12,17].

The noted confounders were included in models in sets to examine their statistical effect on the relative risk measure. The following confounding covariates used in multivariable analyses were measured at year 0, and we assumed that they represented year 1 measures: age at enrollment (<50–59, 60–69, 70–79 y); race (American Indian or Alaska Native, Asian or Pacific Islander, Black or African American, Hispanic/Latino, Whites, and other) and ethnicity (Hispanic/Latino); education (high school or less, some college/technical training, college or some postcollege, and master's degree or higher); annual family income (<$10,000, $10,000–$19,999, $20,000–$34,999, $35,000–$49,999, $50,000–$74,999, $75,000–$99,999, $100,000–$149,999, and ≥$150,000), measured BMI (<18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, 35.0–39.9, ≥40); self-reported physical activity [measured as metabolic equivalent tasks per week (treated as a continuous variable)]; alcohol intake (nondrinker, past drinker, <1 drink/mo, 1 drink/mo to <1 drink/wk, 1 to <7 drinks/wk, and ≥7 drinks/wk); smoking (never smoked, past smoker, and current smoker); hormonal therapy (never used hormones, past hormone user, and current hormone user); diabetes diagnosis ever (yes/no); overall diet quality [Healthy Eating Index (HEI)-2015 (treated as a continuous variable)]; and total energy intake (treated as a continuous variable).

Follow-up and ascertainment of cases

Annual self-administered questionnaires ascertained initial cancer reports, and reported breast cancers were confirmed after a medical record review by trained physician adjudicators at the clinical centers. Final adjudication and coding were performed at the WHI Clinical Coordinating Center by an experienced Surveillance, Epidemiology, and End Results (SEER) coder [18]. Primary site and histology were coded using the International Classification of Diseases for Oncology, Second Edition (ICD-O-2). The completion rate of annual questionnaires was 93%–96% through 2005—the end of the main study period. A large sample size of the WHI OS cohort allowed for performing stratified analyses by tumor stage (invasive and in situ breast cancer) [19,20]. We also performed a stratified analysis by hormone receptor status [estrogen receptor (ER)-positive, ER-negative, progesterone receptor (PR)-positive, and PR-negative). The tumor hormone receptor status was coded using the National Cancer Institute's SEER coding system [21].

Statistical analysis

All participants were followed up from year 1 questionnaire until the date of breast cancer diagnosis (invasive or in situ, whichever was diagnosed first), date of death, loss to follow-up, or 28 February 2020, whichever occurred first. We described the breakfast and after-dinner snack habits by estimating means and standard deviations (SD) for continuous covariates and frequencies and percentages for categorical covariates.

Cox proportional hazard models with time since year 1 examination as the underlying time metric were fitted to estimate HR and 95% CI for the relationship between breakfast meal frequency, after-dinner snack frequencies, and the risk of developing breast cancer. Exposure variables were treated as categorical, time-fixed covariates. Three models were fitted for all outcomes with adjustments for several established risk factors for breast cancer. In model 1, adjustment was made for age and race/ethnicity. Model 2 was additionally adjusted for education, income, physical activity, smoking, alcohol intake, diet quality score (HEI-2015), and energy intake. Furthermore, model 3 accounted for diabetic status, BMI, and hormone therapy. All covariates were measured at year 0 (except primary exposure variables, measured at year 1) and treated as time-fixed covariates. The proportionality assumption was checked by graphical methods and was found not to have been violated. A Wald test of heterogeneity across strata was used to test the overall effect of primary exposure. The α level for the analyses was 0.05.

In addition, we stratified the models as follows: *1*) by BMI (using the median of 27.1 kg/m^2 as a threshold, <27.1 compared with ≥27.1); *2*) by smoking status (ever smokers compared with never smokers); *3*) breakfast meal frequency by after-dinner snack frequency (0–2 times/wk and 3–7 times/wk); and *4*) after-dinner snack frequency by breakfast meal frequency (0–2 times/wk and 3–7 times/wk).

We performed the following sensitivity analyses to inform the interpretation of the results: *1*) excluded all cases within the first 2 y to account for potential reverse causality and *2*) incorporated an inverse probability weight at year 1 to account for potential selection bias into the analysis [16].

We also performed a post hoc analysis by estimating the association of breakfast meal and after-dinner snack frequencies with breast cancer recurrence in women with a history of breast cancer at year 0 (but cancer-free at year 1). Moreover, we compared the estimates after and before adjusting for total energy intake values. We also adjusted the analysis for the number

TABLE 1
Baseline characteristics[1] of eligible participants in the WHI OS population (1994–2020) by after-dinner snacks frequency

	Eat after-dinner snack, times/wk					
	Overall (n = 74,825)	<1 (n = 17,242)	1-2 (n = 20,326)	3-4 (n = 17,903)	5-6 (n = 10,492)	≥7 (n = 8862)
Age at screening, y						
50–59	24,468 (32.7)	4931 (28.6)	6830 (33.6)	5998 (33.5)	3725 (35.5)	2986 (33.7)
60–69	33,222 (44.4)	7518 (43.6)	8943 (44)	8164 (45.6)	4658 (44.4)	3935 (44.4)
70–79	17,135 (22.9)	4793 (27.8)	4533 (22.3)	3760 (21)	2109 (20.1)	1950 (22)
Education						
Did not go to school	75 (0.1)	17 (0.1)	20 (0.1)	18 (0.1)	0 (0)	0 (0)
Grade school (1–4 y)	150 (0.2)	52 (0.3)	20 (0.1)	18 (0.1)	10 (0.1)	18 (0.2)
Grade school (5–8 y)	524 (0.7)	224 (1.3)	142 (0.7)	90 (0.5)	42 (0.4)	53 (0.6)
Some high school (9–11 y)	2020 (2.7)	483 (2.8)	528 (2.6)	465 (2.6)	273 (2.6)	284 (3.2)
High school diploma or GED	11,822 (15.8)	2310 (13.4)	3151 (15.5)	3008 (16.8)	1752 (16.7)	1586 (17.9)
Vocational or training school	6959 (9.3)	1552 (9)	1890 (9.3)	1737 (9.7)	955 (9.1)	851 (9.6)
Some college or associate degree	20,203 (27)	4448 (25.8)	5569 (27.4)	5013 (28)	2759 (26.3)	2410 (27.2)
College graduate or baccalaureate degree	8979 (12)	2310 (13.4)	2480 (12.2)	1987 (11.1)	1259 (12)	931 (10.5)
Some postgraduate or professional	9278 (12.4)	2362 (13.7)	2500 (12.3)	2148 (12)	1270 (12.1)	1028 (11.6)
Master's degree	12,645 (16.9)	2879 (16.7)	3415 (16.8)	2954 (16.5)	1899 (18.1)	1462 (16.5)
Doctoral degree (e.g., PhD, MD, JD)	2245 (3)	603 (3.5)	610 (3)	483 (2.7)	283 (2.7)	239 (2.7)
Race/ethnicity						
Non-Hispanic/ Latino	2592 (3.5)	847 (5)	748 (3.7)	518 (2.9)	258 (2.5)	221 (2.5)
American Indian/ Alaska Native	202 (0.3)	59 (0.3)	57 (0.3)	45 (0.3)	19 (0.2)	22 (0.3)
Asian	2099 (2.8)	527 (3.1)	574 (2.8)	534 (3)	261 (2.5)	203 (2.3)
Native Hawaiian/ Other PI	52 (0.1)	15 (0.1)	19 (0.1)	12 (0.1)	3 (0)	3 (0)
Black	4465 (6)	978 (5.7)	1424 (7.1)	1122 (6.3)	561 (5.4)	380 (4.3)
White	65,581 (88.2)	15,000 (87.7)	17,563 (87)	15,648 (88)	9387 (89.9)	7983 (90.7)
>1 race	770 (1)	155 (0.9)	225 (1.1)	201 (1.1)	101 (1)	88 (1)
Unknown/not reported	1165 (1.6)	378 (2.2)	331 (1.6)	224 (1.3)	105 (1)	127 (1.4)
Family income ($)						
<10,000	2320 (3.1)	603 (3.5)	650 (3.2)	483 (2.7)	294 (2.8)	337 (3.8)
10,000–19,999	7483 (10)	1672 (9.7)	1911 (9.4)	1862 (10.4)	1018 (9.7)	1046 (11.8)
20,000–34,999	16,761 (22.4)	3397 (19.7)	4573 (22.5)	4189 (23.4)	2434 (23.2)	2127 (24)
35,000–49,999	15,115 (20.2)	3207 (18.6)	4147 (20.4)	3724 (20.8)	2182 (20.8)	1817 (20.5)
50,000–74,999	15,339 (20.5)	3414 (19.8)	4207 (20.7)	3652 (20.4)	2287 (21.8)	1755 (19.8)
75,000–99,999	7333 (9.8)	1845 (10.7)	2073 (10.2)	1665 (9.3)	1018 (9.7)	700 (7.9)
100,000–149,999	5387 (7.2)	1517 (8.8)	1463 (7.2)	1217 (6.8)	682 (6.5)	523 (5.9)
≥150,000	3068 (4.1)	983 (5.7)	813 (4)	609 (3.4)	346 (3.3)	301 (3.4)
Do not know	2020 (2.7)	603 (3.5)	467 (2.3)	483 (2.7)	231 (2.2)	257 (2.9)
BMI (kg/m^2)						
Underweight (<18.5)	898 (1.2)	276 (1.6)	203 (1)	179 (1)	94 (0.9)	133 (1.5)
Normal (18.5–24.9)	30,529 (40.8)	8224 (47.7)	8252 (40.6)	6732 (37.6)	3955 (37.7)	3359 (37.9)
Overweight (25.0–29.9)	25,441 (34)	5517 (32)	7033 (34.6)	6320 (35.3)	3641 (34.7)	2951 (33.3)
Obesity I (30.0–34.9)	11,373 (15.2)	2086 (12.1)	3130 (15.4)	2972 (16.6)	1752 (16.7)	1462 (16.5)
Obesity II (35.0–39.9)	4115 (5.5)	707 (4.1)	1098 (5.4)	1074 (6)	671 (6.4)	576 (6.5)
Extreme obesity III (≥40)	2469 (3.3)	448 (2.6)	610 (3)	627 (3.5)	378 (3.6)	381 (4.3)
Diabetes ever	3666 (4.9)	621 (3.6)	894 (4.4)	913 (5.1)	567 (5.4)	691 (7.8)
HRT use ever						

(*continued on next page*)

TABLE 1 (*continued*)

	Eat after-dinner snack, times/wk					
	Overall (n = 74,825)	<1 (n = 17,242)	1-2 (n = 20,326)	3-4 (n = 17,903)	5-6 (n = 10,492)	≥7 (n = 8862)
Never used hormones	20,801 (27.8)	4879 (28.3)	5671 (27.9)	4923 (27.5)	2812 (26.8)	2543 (28.7)
Past hormone user	14,666 (19.6)	3345 (19.4)	3862 (19)	3616 (20.2)	2014 (19.2)	1826 (20.6)
Current hormone user	39,358 (52.6)	9018 (52.3)	10,793 (53.1)	9363 (52.3)	5666 (54)	4493 (50.7)
Smoking status						
Never smoked	37,712 (50.4)	8742 (50.7)	10,671 (52.5)	9166 (51.2)	5089 (48.5)	4059 (45.8)
Past smoker	32,549 (43.5)	7483 (43.4)	8415 (41.4)	7645 (42.7)	4805 (45.8)	4236 (47.8)
Current smoker	4490 (6)	1000 (5.8)	1240 (6.1)	1110 (6.2)	598 (5.7)	567 (6.4)
Alcohol intake						
Nondrinker	7597 (10.2)	1816 (10.6)	2068 (10.2)	1814 (10.2)	1028 (9.9)	871 (9.9)
Past drinker	13,177 (17.7)	2,526 (14.8)	3395 (16.8)	3191 (17.9)	1924 (18.4)	2141 (24.3)
<1 drink/mo	8554 (11.5)	1425 (8.3)	2301 (11.4)	2208 (12.4)	1417 (13.6)	1203 (13.7)
<1 drink/wk	15,002 (20.2)	2793 (16.3)	4122 (20.4)	3901 (21.9)	2352 (22.5)	1834 (20.8)
1–7 drinks/wk	19,881 (26.8)	4716 (27.6)	5623 (27.9)	4811 (27.1)	2749 (26.3)	1982 (22.5)
>7 drinks/wk	9807 (13.2)	3746 (21.9)	2591 (12.8)	1790 (10.1)	932 (8.9)	748 (8.5)
How many mammograms in the last 5 y?						
1	4389 (5.9)	1081 (6.3)	1154 (5.7)	1020 (5.7)	592 (5.7)	542 (6.2)
2	8370 (11.3)	1871 (10.9)	2425 (12)	1995 (11.2)	1132 (10.9)	947 (10.8)
3	10,061 (13.5)	2282 (13.3)	2843 (14.1)	2409 (13.5)	1369 (13.1)	1158 (13.2)
4	12,318 (16.6)	2633 (15.4)	3422 (17)	3095 (17.4)	1790 (17.2)	1378 (15.7)
≥5	34,157 (46)	7941 (46.4)	9039 (44.8)	8095 (45.5)	4909 (47)	4173 (47.4)
Total dietary energy intake (kcal/d)	1573 ± 590.1	1486.1 ± 556.8	1526.4 ± 566.4	1587.9 ± 586.4	1659.8 ± 616.6	1713.3 ± 638.4
Total HEI-2015 score	67.3 ± 10.2	68.7 ± 10	67.4 ± 10.1	66.9 ± 10.1	66.4 ± 10.4	66.2 ± 10.7
Total energy expend from recreational physical activity (MET-h/wk)	14.0 ± 14.4	15.8 ± 15.5	14 ± 14.3	13.2 ± 13.7	13.1 ± 13.6	13.4 ± 14.2
Eat breakfast (times/wk)						
<1	4306 (5.4)	1828 (10.6)	915 (4.5)	609 (3.4)	315 (3)	354 (4)
1–2	5133 (6.6)	1259 (7.3)	1890 (9.3)	931 (5.2)	504 (4.8)	346 (3.9)
3–4	417 (5.5)	759 (4.4)	1179 (5.8)	1182 (6.6)	567 (5.4)	408 (4.6)
5–6	9834 (13.2)	1793 (10.4)	2805 (13.8)	2847 (15.9)	1742 (16.6)	665 (7.5)
≥7	51,435 (69.3)	11,587 (67.2)	13,537 (66.6)	12,335 (68.9)	7355 (70.1)	7090 (80)
Gail 5-year risk score	1.8 ± 1	1.9 ± 1	1.8 ± 1	1.8 ± 1	1.8 ± 1	1.8 ± 1

Values are frequency (%) or mean ± SD, if noted.

HEI, Healthy Eating Index; MET, metabolic equivalent of task; SD, standard deviation; WHI OS, Women's Health Initiative Observational Study.

[1] Baseline is year 1 of the WHI OS follow-up, and characteristics are age, race/ethnicity, education, income, diabetes status, hormone therapy, BMI, physical activity, Gail 5-year risk score were measured at year 0.

of mammograms (1, 2, 3, 4, 5, or more) in the last 5 y. All analyses were performed using SAS 9.4.

Results

The final sample for analyses included 74,825 women, with a mean follow-up of 14.67 y (95% CI: 14.62, 14.72 y), during which 6360 breast cancer cases were reported. Of all included study participants, 23.0% (n = 17,242) ate after dinner never or less than once a week, and 11.8% (n = 8862) consumed after-dinner meal 7 or more times a week (Table 1). Only 5.8% (n = 4306) women never ate breakfast or ate it less than once a week, and 68.7% (n = 51,435) consumed breakfast 7 or more times a week (Table 2). Among women who did not consume breakfast regularly (never or less than once a week), 42.3% were aged 60–69 y, and 37.0% were within the normal BMI range (18.5–24.9 kg/m^2). More White than Black women skipped breakfast (Table 2). More regular breakfast consumption was associated with a higher overall diet quality. On the contrary, more regular after-dinner snack consumption was associated with a lower overall diet quality (Table 1). Those who ate after dinner daily had a slightly lower income, were mainly White women, and had a slightly higher proportion of smokers (Table 1). Overall, those who consumed after-dinner snacks 7 or more times a week had, on average, a 200-kcal/d greater energy consumption than those who avoided after-dinner snacks. Moreover, those who avoided after-dinner snacks consumed more alcohol and exercised more than those who ate after-dinner snacks daily (Table 1).

The incidence rate of developing all breast cancers (total of invasive and in situ) in the WHI OS was 5.3 cases per 1000 person-y among those who consumed breakfast every day and 5.5 cases per 1000 person-y among those who avoided eating after-dinner snacks from 1997 to 28 February 2020 (Tables 3 and 4). The HR (95% CI) (model 3) for consuming breakfast daily (7 times/wk) compared with avoiding breakfast (<1 time/wk) was 1.04 (95% CI: 0.9, 1.19) for invasive breast cancer risk (Table 3). For in situ breast cancer risk, compared

TABLE 2
Baseline characteristics[1] of eligible participants in the WHI OS population (1994–2020) by breakfast frequency

	Eat breakfast (times/wk)					
	Overall (n = 74,828)	<1 (n = 4306)	1–2 (n = 5133)	3–4 (n = 4118)	5–6 (n = 9834)	≥7 (n = 51,435)
Age at screening						
50–59	24,468 (32.7)	1520 (35.3)	2248 (43.8)	1836 (44.6)	4091 (41.6)	14,813 (28.8)
60–69	33,222 (44.4)	1821 (42.3)	1956 (38.1)	1754 (42.6)	4111 (41.8)	23,557 (45.8)
70–79	17,135 (22.9)	960 (22.3)	929 (18.1)	527 (12.8)	1632 (16.6)	13,064 (25.4)
Education						
Did not go to school	75 (0.1)	4 (0.1)	0 (0)	8 (0.2)	0 (0)	0 (0)
Grade school (1–4 y)	150 (0.2)	17 (0.4)	26 (0.5)	8 (0.2)	10 (0.1)	51 (0.1)
Grade school (5–8 y)	524 (0.7)	90 (2.1)	82 (1.6)	33 (0.8)	59 (0.6)	257 (0.5)
Some high school (9–11 y)	2020 (2.7)	258 (6)	293 (5.7)	152 (3.7)	295 (3)	1080 (2.1)
High school diploma or GED	11,822 (15.8)	887 (20.6)	903 (17.6)	725 (17.6)	1514 (15.4)	7767 (15.1)
Vocational or training school	6959 (9.3)	474 (11)	631 (12.3)	445 (10.8)	954 (9.7)	4526 (8.8)
Some college or associate degree	20,203 (27)	1236 (28.7)	1509 (29.4)	1243 (30.2)	2852 (29)	13,373 (26)
College graduate or baccalaureate degree	8979 (12)	400 (9.3)	513 (10)	416 (10.1)	1092 (11.1)	6532 (12.7)
Some postgraduate or professional	9278 (12.4)	357 (8.3)	477 (9.3)	445 (10.8)	1180 (12)	6789 (13.2)
Master's degree	12,645 (16.9)	495 (11.5)	580 (11.3)	535 (13)	1583 (16.1)	9413 (18.3)
Doctoral degree (e.g., PhD, MD, JD)	2245 (3)	82 (1.9)	113 (2.2)	107 (2.6)	295 (3)	1646 (3.2)
Race/ethnicity						
Non-Hispanic/ Latino	2592 (3.5)	301 (7)	382 (7.5)	232 (5.7)	430 (4.4)	1247 (2.4)
American Indian/ Alaska Native	202 (0.3)	21 (0.5)	39 (0.8)	25 (0.6)	31 (0.3)	86 (0.2)
Asian	2099 (2.8)	98 (2.3)	185 (3.6)	109 (2.7)	315 (3.2)	1392 (2.7)
Native Hawaiian/ Other PI	52 (0.1)	4 (0.1)	7 (0.1)	5 (0.1)	9 (0.1)	27 (0.1)
Black	4465 (6)	573 (13.4)	677 (13.3)	617 (15.1)	921 (9.4)	1677 (3.3)
White	65,581 (88.2)	3403 (79.6)	3939 (77.3)	3179 (77.7)	8143 (83.4)	46,917 (91.8)
More than 1 race	770 (1)	38 (0.9)	67 (1.3)	54 (1.3)	140 (1.4)	471 (0.9)
Unknown/not reported	1165 (1.6)	136 (3.2)	184 (3.6)	101 (2.5)	202 (2.1)	542 (1.1)
Family income ($)						
<10,000	2320 (3.1)	301 (7)	313 (6.1)	181 (4.4)	364 (3.7)	1234 (2.4)
10,000–19,999	7483 (10)	637 (14.8)	652 (12.7)	478 (11.6)	964 (9.8)	4783 (9.3)
20,000–34,999	16,761 (22.4)	1059 (24.6)	1211 (23.6)	893 (21.7)	2095 (21.3)	11,470 (22.3)
35,000–49,999	15115 (20.2)	814 (18.9)	965 (18.8)	852 (20.7)	1967 (20)	10,493 (20.4)
50,000–74,999	15,339 (20.5)	710 (16.5)	924 (18)	795 (19.3)	2016 (20.5)	10,853 (21.1)
75,000–99,999	7333 (9.8)	289 (6.7)	416 (8.1)	375 (9.1)	1013 (10.3)	5195 (10.1)
100,000–149,999	5387 (7.2)	211 (4.9)	334 (6.5)	272 (6.6)	747 (7.6)	3858 (7.5)
≥150,000	3068 (4.1)	133 (3.1)	159 (3.1)	169 (4.1)	413 (4.2)	2160 (4.2)
Do not know	2020 (2.7)	151 (3.5)	164 (3.2)	103 (2.5)	256 (2.6)	1389 (2.7)
BMI (kg/m^2)						
Underweight (<18.5)	898 (1.2)	65 (1.5)	56 (1.1)	37 (0.9)	59 (0.6)	669 (1.3)
Normal (18.5–24.9)	30,529 (40.8)	1593 (37)	1781 (34.7)	1330 (32.3)	3452 (35.1)	22,323 (43.4)
Overweight (25.0–29.9)	25,441 (34)	1399 (32.5)	1730 (33.7)	1400 (34)	3521 (35.8)	17,385 (33.8)
Obesity I (30.0–34.9)	11,373 (15.2)	745 (17.3)	888 (17.3)	758 (18.4)	1711 (17.4)	7304 (14.2)
Obesity II (35.0–39.9)	4115 (5.5)	289 (6.7)	400 (7.8)	362 (8.8)	679 (6.9)	2417 (4.7)
Extreme obesity III (≥40)	2469 (3.3)	211 (4.9)	272 (5.3)	231 (5.6)	413 (4.2)	1337 (2.6)
Diabetes ever	3666 (4.9)	233 (5.4)	272 (5.3)	165 (4)	413 (4.2)	2623 (5.1)
HRT use ever						

(continued on next page)

TABLE 2 (*continued*)

	Eat breakfast (times/wk)					
	Overall (n = 74,828)	<1 (n = 4306)	1–2 (n = 5133)	3–4 (n = 4118)	5–6 (n = 9834)	≥7 (n = 51,435)
Never used hormones	20,801 (27.8)	1451 (33.7)	1617 (31.5)	1223 (29.7)	2734 (27.8)	13,836 (26.9)
Past hormone user	14,666 (19.6)	960 (22.3)	1068 (20.8)	828 (20.1)	1986 (20.2)	9824 (19.1)
Current hormone user	39,358 (52.6)	1895 (44)	2448 (47.7)	2067 (50.2)	5114 (52)	27,775 (54)
Smoking status						
Never smoked	37,712 (50.4)	1886 (43.8)	2341 (45.6)	1766 (42.9)	4691 (47.7)	27,003 (52.5)
Past smoker	32,549 (43.5)	1813 (42.1)	2130 (41.5)	1828 (44.4)	4455 (45.3)	22,323 (43.4)
Current smoker	4490 (6)	607 (14.1)	667 (13)	523 (12.7)	688 (7)	2057 (4)
Alcohol intake						
Nondrinker	7597 (10.2)	524 (12.3)	592 (11.6)	381 (9.3)	1002 (10.3)	5098 (10)
Past drinker	13,177 (17.7)	945 (22.1)	1088 (21.3)	828 (20.2)	1689 (17.3)	8627 (16.9)
<1 drink/mo	8554 (11.5)	508 (11.9)	638 (12.5)	543 (13.3)	1182 (12.1)	5683 (11.1)
<1 drink/wk	15,002 (20.2)	783 (18.3)	969 (19)	758 (18.5)	1997 (20.5)	10,495 (20.5)
1–7 drinks/wk	19,881 (26.8)	914 (21.4)	1169 (22.9)	1053 (25.8)	2656 (27.2)	14,089 (27.6)
>7 drinks/wk	9807 (13.2)	563 (13.2)	617 (12.1)	507 (12.4)	1183 (12.1)	6937 (13.6)
How many mammograms in the last 5 y?						
1	4389 (5.9)	386 (9)	439 (8.6)	369 (9)	673 (6.9)	2522 (4.9)
2	8370 (11.3)	610 (14.3)	684 (13.4)	530 (13)	1177 (12.1)	5369 (10.5)
3	10,061 (13.5)	575 (13.5)	707 (13.9)	596 (14.6)	1386 (14.2)	6797 (13.3)
4	12,318 (16.6)	631 (14.8)	781 (15.3)	645 (15.8)	1740 (17.8)	8521 (16.7)
≥5	34,157 (46)	1615 (37.8)	1961 (38.5)	1616 (39.5)	4065 (41.7)	24,900 (48.7)
Total dietary energy intake (kcal/d)	1573 ± 590.1	1489.8 ± 649.7	1533.2 ± 665.2	1569.9 ± 662	1551 ± 618.5	1588 ± 563.8
Total HEI-2015 score	67.3 ± 10.2	63.5 ± 11.1	63.1 ± 10.7	63.2 ± 10.3	66 ± 10.1	68.6 ± 9.8
Total energy expend from recreational physical activity (MET-h/wk)	14.0 ± 14.4	12.6 ± 15.05	11.8 ± 14.3	12 ± 14.6	13.2 ± 14.2	14.7 ± 14.3
Eat after-dinner (times/wk)						
<1	17,825 (22.9)	1951 (45.3)	1304 (25.4)	762 (18.5)	1780 (18.1)	11,419 (22.2)
1–2	20,326 (27.2)	986 (22.9)	1976 (38.5)	1186 (28.8)	2803 (28.5)	13,425 (26.1)
3–4	17,603 (24.1)	650 (15.1)	975 (19)	1198 (29.1)	2862 (29.1)	12,293 (23.9)
5–6	10,492 (14.1)	344 (8)	529 (10.3)	572 (13.9)	1741 (17.7)	7304 (14.2)
≥7	8862 (11.7)	375 (8.7)	354 (6.9)	403 (9.8)	659 (6.7)	6944 (13.5)
Gail 5-year risk score	1.8 ± 1	1.7 ± 1	1.6 ± 1	1.6 ± 0.9	1.7 ± 1	1.9 ± 1

Values are frequency (%) or mean ± SD, if noted.

HEI, Healthy Eating Index; MET, metabolic equivalent of task; SD, standard deviation; WHI OS, Women's Health Initiative Observational Study.

[1] Baseline is year 1 of the WHI OS follow-up, and characteristics are age, race/ethnicity, education, income, diabetes status, hormone therapy, BMI, physical activity, Gail 5-year risk score were measured at year 0.

with women who avoided breakfast meals (<1 time/wk), there was a stepwise higher HR for women with a higher breakfast frequency, with a statistical trend in a linear test but wide CIs (Table 3).

The HR for avoiding after-dinner snacks (<1 time/wk) compared with consuming after-dinner snacks daily (7 times/wk) was 0.97 (95% CI: 0.87, 1.08) for invasive breast cancer and 1.12 (95% CI: 0.89, 1.42) for in situ breast cancer risk (Table 4).

For in situ breast cancer risk, women with BMI ≥27.11 kg/m^2, compared with women who avoided breakfast meals (<1 time/wk), those who consumed breakfast 1–2 times/wk recorded an HR of 1.81 (95% CI: 0.87, 3.79), those who consumed breakfast 3–4 times/wk recorded an HR of 2.11 (95% CI: 1.01, 4.39), those who consumed breakfast 5–6 times/wk recorded an HR of 2.13 (95% CI: 1.09, 4.17), and those who consumed breakfast 7 times/wk recorded an HR of 2.38 (95% CI: 1.26, 4.48) (P = .006, Wald test) (Table 5).

Overall, there was no effect modification by smoking; however, never smokers who consumed more regular (5–6 times/wk) and habitual breakfast (7 or more times/wk) exhibited a higher risk of in situ breast cancer diagnosis than those never smokers who avoided breakfast (HR: 1.83; 95% CI: 1.01, 3.48; and HR: 2.00; 95% CI: 1.09, 3.65, respectively) (Table 6). When women who consumed after-dinner snacks 0–2 times/wk consumed breakfast 0–2 times/wk, they recorded an HR of 0.78 (95% CI: 0.58, 0.98) for in situ breast cancer diagnosis compared with women who consumed breakfast 3–7 times/wk (Supplemental Table 1).

The stratified analysis by tumor receptor status showed that compared with consuming after-dinner snacks ≥7 times/wk, consuming after-dinner snacks <1 time/wk had no differential effect on tumor receptor status, resulting in an HR of 1.04 (95% CI: 1.01, 1.07) for PR-positive, PR-negative, ER-positive, and ER-negative cases (Supplemental Table 2). Similarly, compared with consuming breakfast <1 time/wk, consuming breakfast ≥7 times/wk had no differential effect on tumor receptor status, resulting in an HR of 1.02 (95% CI: 0.98, 1.05) for PR-positive, PR-negative, ER-positive, and ER-negative cases.

TABLE 3
Relative risk[1] of breast cancers (all, invasive, and in situ) by breakfast frequency, Women's Health Initiative Observational Study, 1994–2020

ModeH2	Breakfast frequency (times/wk)	Person-y	All breast			Invasive			In situ		
			Cases (*n*)	HR (95% CI)	*P*-trend[3]	Cases (*n*)	HR (95% CI)	*P*-trend[3]	Cases (*n*)	HR (95% CI)	*P*-trend[3]
1	<1	68,763.1	310	Reference	0.006	263	Reference	0.06	47	Reference	0.007
	1–2	82,737.6	370	1.01 (0.86, 1.19)		313	1 (0.83, 1.19)		62	1.16 (0.77, 1.74)	
	3–4	67,063.3	321	1.05 (0.89, 1.24)		276	1.03 (0.86, 1.24)		58	1.27 (0.84, 1.92)	
	5–6	159,315.5	846	1.12 (0.98, 1.29)		718	1.11 (0.95, 1.29)		138	1.28 (0.9, 1.82)	
	≥7	847,738.2	4474[4]	1.13 (1, 1.28)		3703	1.09 (0.96, 1.25)		874	1.43 (1.04, 1.97)	
2	<1			Reference	0.07		Reference	0.25		Reference	0.04
	1–2			0.99 (0.84, 1.17)			0.98 (0.82, 1.18)			1.12 (0.74, 1.69)	
	3–4			1.02 (0.86, 1.2)			1 (0.83, 1.21)			1.24 (0.82, 1.88)	
	5–6			1.09 (0.95, 1.25)			1.07 (0.92, 1.25)			1.23 (0.86, 1.77)	
	≥7			1.08 (0.95, 1.23)			1.05 (0.92, 1.21)			1.34 (0.97, 1.85)	
3	<1			Reference	0.05		Reference	0.16		Reference	0.04
	1–2			0.98 (0.83, 1.16)			0.98 (0.82, 1.17)			1.09 (0.72, 1.64)	
	3–4			0.99 (0.84, 1.18)			0.98 (0.82, 1.19)			1.19 (0.78, 1.8)	
	5–6			1.06 (0.92, 1.23)			1.06 (0.9, 1.24)			1.20 (0.8, 1.65)	
	≥7			1.06 (0.93, 1.2)			1.04 (0.9, 1.19)			1.25 (0.91, 1.74)	

HEI, Healthy Eating Index; WHI OS, Women's Health Initiative Observational Study.
[2]Model 1 was adjusted for age and race/ethnicity; model 2 for model 1 variables + education, income, physical activity, smoking, alcohol intake, diet quality score (HEI-2015), and energy intake; and model 3 for model 2 + diabetes status, BMI, and hormone therapy.
[1] Calculated using Cox proportional hazards models and presented as HRs and 95% confidence intervals.
[3] *P* values for Wald test of general heterogeneity, with *df* = number of categories − 1. The α level for the analyses was 0.05.
[4] Incidence rate of developing breast cancer (all) in the WHI OS was 5.3 cases per 1000 person-y among those who consumed breakfast every day from 1997 to 28 February 2020.

Excluding breast cancer diagnosis during the first 2 y of the follow-up did not result in any noticeable change in the estimates (Supplemental Table 3). Using inverse probability weights adjusted for age, self-identified race/ethnicity, education, income, physical activity, smoking, alcohol intake, diet quality score (HEI-2015) [22], energy intake, diabetic status, and BMI resulted in a greater magnitude of association between breakfast consumption and in situ breast cancer risk and a stronger statistical signal; however, the direction of the association remained the same as in the conventional analysis (Supplemental Table 4).

The post hoc analysis that evaluated the association between after-dinner snacks, breakfast, and breast cancer recurrence risk among women with a history of breast cancer suggested no association between those meals and disease recurrence risk (Supplemental Table 5). We also assessed whether adjusting for the number of mammograms in the past 5 y affected the association between meal frequencies and breast cancer risk (Supplemental Table 6). This adjustment did not change the magnitude or direction of the association estimates, and there was no association of breakfast frequency with in situ breast cancer incidence, and the statistical test for trend ($P = 0.06$, Wald test) suggested no more residual influence of breakfast consumption on risk of in situ breast cancer. In addition, after comparing the estimates before and after adjustment for total energy intake, we found no material difference between them.

Discussion

To our knowledge, this study is one of the first to assess the association of breakfast meals and after-dinner snacks with the risk of breast cancer in a large cohort of postmenopausal women. Overall, we observed no association between a higher breakfast intake frequency and risk for invasive or in situ breast cancer and no/infrequent breakfast intake. However, for each higher category of breakfast intake, there were higher point estimates for risk of in situ breast cancer. Finally, there was no association between the frequency of after-dinner snacks/eating occasions and the risk for breast cancer.

The suggestive association of increased risk of in situ breast cancer linked with regular breakfast consumption could reflect confounding by systematic surveillance behavior of women. Indeed, this study has shown that women who consumed breakfast regularly were also more likely to get a mammogram and a physical breast examination (Table 1). Furthermore, we saw that those who regularly consumed breakfast had a healthier

TABLE 4
Relative risk[1] of breast cancer (all, invasive, and in situ) by after-dinner snacks frequency, Women's Health Initiative Observational Study, 1994–2020

ModeH2	After-dinner snacks frequency (times/wk)	Person-y	All breast			Invasive			In situ		
			Cases (*n*)	HR (95% CI)	*P*-trend[3]	Cases (*n*)	HR (95% CI)	*P*-trend[3]	Cases (*n*)	HR (95% CI)	*P*-trend[3]
1	<1	275,214.0	1500[4]	1.02 (0.93, 1.12)	0.35	1241	0.99 (0.9, 1.1)	0.44	276	1.17 (0.94, 1.46)	0.55
	1-2	329,880.3	1768	1.01 (0.93, 1.11)		1484	1 (0.91, 1.11)		305	1.03 (0.83, 1.29)	
	3-4	287,947.0	1468	0.97 (0.88, 1.07)		1217	0.95 (0.86, 1.05)		269	1.03 (0.82, 1.29)	
	5-6	169,770.0	881	0.98 (0.89, 1.09)		713	0.94 (0.84, 1.05)		189	1.2 (0.95, 1.53)	
	≥7	138,659.8	744	Reference		629	Reference		124	Reference	
2	<1			0.98 (0.89, 1.08)	0.87		0.96 (0.87, 1.07)	0.87		1.1 (0.87, 1.38)	0.95
	1-2			1 (0.91, 1.1)			0.99 (0.9, 1.1)			1 (0.8, 1.25)	
	3-4			0.96 (0.88, 1.06)			0.94 (0.85, 1.05)			1.02 (0.81, 1.27)	
	5-6			0.97 (0.88, 1.08)			0.93 (0.83, 1.04)			1.18 (0.93, 1.5)	
	≥7			Reference			Reference			Reference	
3	<1			0.99 (0.9, 1.1)	0.85		0.97 (0.87, 1.08)	0.84		1.12 (0.89, 1.42)	0.99
	1-2			1 (0.91, 1.1)			0.98 (0.89, 1.09)			1.02 (0.81, 1.28)	
	3-4			0.96 (0.87, 1.06)			0.94 (0.84, 1.04)			1.02 (0.81, 1.29)	
	5-6			0.97 (0.88, 1.08)			0.93 (0.83, 1.04)			1.19 (0.93, 1.53)	
	≥7			Reference			Reference			Reference	

[2]Model 1 was adjusted for age and race/ethnicity; model 2 for model 1 variables + education, income, physical activity, smoking, alcohol intake, diet quality score (HEI-2015), and energy intake; and model 3 for model 2 + diabetes status, BMI, and hormone therapy.
[1] Calculated using Cox proportional hazards models and presented as HRs and 95% confidence intervals.
[3] *P* values for Wald test of general heterogeneity, with *df* = number of categories − 1. The α level for the analyses was 0.05.
[4] Incidence rate of developing breast cancer (all) in the WHI OS was 5.3 cases per 1000 person-y among those who avoided eating after dinner every day from 1997 to 28 February 2020.

diet, exercised more, and were less likely to smoke. These factors serve as a proxy for the health consciousness of women more likely to take advantage of breast cancer screening [23,24]. Having undergone a mammogram examination is one of the strongest and most prevalent risk factors associated with diagnosing in situ breast cancers [25]. Regular cancer screening allows diagnosis of an earlier stage of tumor progression (in situ), which increases the chances of preventing invasive breast cancer [26]. Thus, some of the tumors identified at an earlier stage would not progress to an invasive stage in such a scenario, creating an artifactual "harm" of regular breakfast consumption.

A post hoc adjustment for the number of mammograms in the last 5 y attenuated the statistical trend in the association between breakfast frequency and in situ breast cancer. Speculatively, this supports the plausible explanation that the positive trend between breakfast frequency and in situ breast cancer diagnosis is an artifact of health-conscientious behavior.

Higher BMI is reported to be associated with increased mammographic sensitivity, potentially leading to the overestimated relationship between BMI and the risk of developing in situ breast cancer [27,28]. This might explain a higher magnitude of association estimates between breakfast consumption and in situ breast cancer risk observed among participants with a BMI of >27 kg/m^2.

Similar to our findings, a large prospective cohort study in 2018 concluded no association between cancer risk and the number of eating episodes, nighttime fasting duration, and time of first eating episode [29]. In a cross-sectional study, Marinac et al. [9] suggested that a longer nighttime duration was significantly associated with improved glycemic regulation, particularly noting that each 3-h increase in nighttime fasting duration was associated with approximately a 20% reduced odds of elevated HbA1c levels. Although there is contradicting evidence on the association between HbA1c and risk of breast cancer, we addressed the potential association between prolonged night fast and risk of breast cancer in this study [30,31]. Night fasting time can be prolonged by avoiding after-dinner snacks, breakfast, or both. Supporting the findings of the abovementioned study, we observed that participants who avoided breakfast and did not eat after-dinner snacks regularly had a lower in situ breast cancer risk. However, there was no association between skipping after-dinner snacks and invasive breast cancer risk in those participants who did not eat breakfast regularly.

Another study concluded that fasting less than 13 h per night was associated with an increased risk of breast cancer recurrence compared with fasting ≥13h/night [10]. In our post hoc analysis, we assessed the risk of breast cancer recurrence among

TABLE 5
Stratified analysis of the association between meal frequencies and risk of breast cancer by BMI, Women's Health Initiative Observational Study, 1994–2020.

BMI[1]	Meal	Frequency (times/wk)	All breast			Invasive			In situ		
			Cases (*n*)	HR (95% CI)[2]	*P*-trend[3]	Cases (*n*)	HR (95% CI)[2]	*P*-trend[3]	Cases (*n*)	HR (95%CI)[2]	*P*-trend[3]
Below median	After-dinner snack	<1	1003	1.02 (0.9, 1.16)	0.21	829	1 (0.87, 1.15)	0.26	196	1.17 (0.87, 1.57)	0.30
		1–2	1023	1.01 (0.89, 1.14)		855	1 (0.87, 1.14)		182	1.03 (0.77, 1.38)	
		3–4	808	0.95 (0.83, 1.08)		657	0.92 (0.8, 1.06)		158	1.04 (0.77, 1.4)	
		5–6	475	0.93 (0.81, 1.08)		382	0.9 (0.77, 1.06)		100	1.05 (0.76, 1.46)	
		≥7	394	Reference		330	Reference		70	Reference	
	Breakfast	<1	179	Reference	0.72	149	Reference	0.78	31	Reference	0.76
		1–2	185	0.94 (0.75, 1.17)		154	0.97 (0.76, 1.24)		35	0.86 (0.51, 1.43)	
		3–4	151	0.93 (0.73, 1.18)		126	0.95 (0.73, 1.24)		30	0.94 (0.56, 1.59)	
		5–6	435	1.04 (0.86, 1.26)		363	1.09 (0.88, 1.34)		76	0.89 (0.58, 1.38)	
		≥7	2753	0.99 (0.84, 1.17)		2261	1.01 (0.84, 1.22)		534	0.96 (0.66, 1.41)	
Above median	After-dinner snack	<1	471	0.91 (0.79, 1.04)	0.18	395	0.9 (0.76, 1.06)	0.28	79	0.92 (0.63, 1.34)	0.15
		1–2	717	1 (0.88, 1.14)		614	0.98 (0.84, 1.14)		112	0.96 (0.68, 1.36)	
		3–4	661	0.97 (0.85, 1.1)		561	0.96 (0.82, 1.12)		107	0.96 (0.68, 1.36)	
		5–6	406	1 (0.87, 1.15)		329	0.97 (0.82, 1.15)		86	1.34 (0.93, 1.91)	
		≥7	336	Reference		290	Reference		53	Reference	
	Breakfast	<1	130	Reference	0.008	117	Reference	0.07	13	Reference	0.006
		1–2	172	1.08 (0.84, 1.38)		144	1.02 (0.78, 1.32)		30	1.81 (0.87, 3.79)	
		3–4	162	1.11 (0.87, 1.43)		139	1.04 (0.8, 1.36)		26	2.11 (1.01, 4.39)	
		5–6	393	1.15 (0.93, 1.43)		332	1.07 (0.85, 1.35)		65	2.13 (1.09, 4.17)	
		≥7	1743	1.26 (1.05, 1.5)		1457	1.14 (0.93, 1.4)		303	2.38 (1.26, 4.48)	

HEI, Healthy Eating Index.
[1] Median BMI is 27.11 kg/m^2.
[2] Calculated using Cox proportional hazards models and presented as HRs and 95% CIs. The models were adjusted for age, race/ethnicity, education, income, physical activity, smoking, alcohol intake, diet quality score (HEI-2015), energy intake, and diabetic status.
[3] *P* value for Wald test of general heterogeneity with *df* = number of categories −1. The α level for the analyses was 0.05.

women with a history of breast cancer at year 1. We found that regularly consuming after-dinner snacks and breakfast was not associated with an increased risk of breast cancer recurrence compared with avoiding those meals. A small number of women with a history of breast cancer were included in the analysis, which could result in type II error.

One of the primary strengths of this study was the large sample of postmenopausal women in the WHI OS cohort, which made it feasible to examine incremental differences in breakfast and after-dinner snacks as risk factors for breast cancer as allowed for performing stratified analyses by tumor stages. In addition, a breast cancer diagnosis was confirmed by a medical record review, and all cases were adjudicated. Careful adjustment for confounders, including validated dietary data, was also advantageous for this analysis. A prospective design of this study, excluding all prevalent breast cancer cases at the baseline, allowed producing the estimates for breast cancer-free subjects. The mean 14.7-year follow-up period provided a considerable latency period for potential disease occurrence.

Owing to the study's observational nature, the results should only be generalized to the healthy, postmenopausal women population. Another limitation of this study is the participants' self-reported meal frequency and other confounding variables, which might be subject to measurement error. Single breakfast and after-dinner snack exposure measures may not fully reflect long-term associations with breast cancer risks. Furthermore, it is essential to note that breakfast and after-dinner snack frequency could serve as a proxy for circadian rhythms, which are the actual correlates of cancer development and that these also depend on many other lifestyle and environmental factors. In addition, although this analysis adjusts for the overall diet quality, the quality of the individual meals was not assessed and could not be controlled for. Although we attempted to control confounding, residual confounding cannot be ruled out.

TABLE 6
Stratified analysis of the association between meal frequencies and risk of breast cancer by smoking status, Women's Health Initiative Observational Study, 1994–2020.

Smoking ever	Meal	Frequency (times/wk)	All breast			Invasive			In situ		
			Cases (*n*)	HR (95% CI)[1]	*P*-trend[2]	Cases (*n*)	HR (95% CI)[1]	*P*-trend[2]	Cases (*n*)	HR (95% CI)[1]	*P*-trend[2]
No	After-dinner snack	<1	700	1.02 (0.89, 1.18)	0.87	575	0.99 (0.85, 1.16)	0.97	138	1.22 (0.87, 1.71)	0.52
		1–2	838	1 (0.87, 1.15)		704	0.98 (0.85, 1.14)		147	1.08 (0.77, 1.5)	
		3–4	730	1.01 (0.88, 1.16)		602	0.99 (0.85, 1.15)		137	1.11 (0.79, 1.56)	
		5–6	416	1.02 (0.87, 1.19)		335	0.97 (0.82, 1.15)		86	1.21 (0.84, 1.74)	
		≥7	323	Reference		273	Reference		55	Reference	
	Breakfast	<1	124	Reference	0.06	110	Reference	0.3347	14	Reference	0.002
		1–2	157	0.97 (0.75, 1.26)		133	0.96 (0.74, 1.26)		24	1.19 (0.56, 2.52)	
		3–4	127	1.02 (0.78, 1.33)		106	1 (0.76, 1.33)		22	1.69 (0.81, 3.54)	
		5–6	352	1.04 (0.84, 1.3)		292	1 (0.79, 1.26)		65	1.83 (1.01, 3.48)	
		≥7	2247	1.11 (0.91, 1.35)		1848	1.06 (0.86, 1.3)		438	2 (1.09, 3.65)	
Yes	After-dinner snack	<1	768	0.97 (0.85, 1.11)	0.80	644	0.96 (0.83, 1.1)	0.7015	136	1 (0.73, 1.36)	0.57
		1–2	891	1.02 (0.9, 1.15)		756	1.01 (0.88, 1.16)		145	0.95 (0.7, 1.29)	
		3–4	725	0.92 (0.81, 1.05)		607	0.9 (0.78, 1.04)		123	0.93 (0.68, 1.27)	
		5–6	460	0.95 (0.83, 1.1)		373	0.91 (0.78, 1.07)		98	1.15 (0.84, 1.6)	
		≥7	404	Reference		345	Reference		67	Reference	
	Breakfast	<1	183	Reference	0.22	155	Reference	0.21	29	Reference	0.99
		1–2	198	1.03 (0.83, 1.28)		163	1.04 (0.82, 1.32)		41	1.11 (0.68, 1.82)	
		3–4	184	1 (0.8, 1.25)		158	1.04 (0.81, 1.32)		33	1.06 (0.64, 1.76)	
		5–6	468	1.14 (0.94, 1.37)		398	1.18 (0.96, 1.45)		73	0.95 (0.61, 1.49)	
		≥7	2215	1.09 (0.92, 1.29)		1851	1.11 (0.92, 1.33)		393	1.04 (0.7, 1.54)	

HEI, Healthy Eating Index.
[1] Calculated using Cox proportional hazards models and presented as HRs and 95% CIs. The models were adjusted for age, race/ethnicity, education, income, physical activity, alcohol intake, diet quality score (HEI-2015), energy intake, diabetic status, BMI, and hormone therapy.
[2] *P* value for Wald test of general heterogeneity with *df* = number of categories − 1. The α level for the analyses was 0.05.

In summary, there was no association between the frequency of breakfast meals or after-dinner snacks and the risk of breast cancer in postmenopausal women. There was a suggestive association of an increased risk of in situ breast cancer with a higher frequency of breakfast consumption, which likely reflects residual confounding owing to health conscientiousness and regular breast cancer screening among those who consume breakfast regularly. Nevertheless, the nature of our analysis precludes stronger conclusions or making clinical recommendations.

Data Availability

Data described in the manuscript, code book, and analytic code will be made available on request pending application and approval.

Funding

The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, US Department of Health and Human Services through contracts HHSN268201600018C, HHSN268201600001C, HHSN26820 1600002C, HHSN268201600003C, and HHSN268201600004C.

Author disclosures

The authors report no conflicts of interest.

Acknowledgments

The authors' responsibilities were as follows—VE: designed and conducted the research, performed statistical analyses, wrote the paper, and had primary responsibility for final content; CT, MLN, LJ, SL, KP, MV, RC, DL: other; AOO: designed the research, had primary responsibility for final content, and other; and all authors: read and approved the final version of the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tjnut.2023.02.003.

References

[1] F. Menegaux, T. Truong, A. Anger, E. Cordina-Duverger, F. Lamkarkach, P. Arveux, et al., Night work and breast cancer: a population-based case-control study in France (the CECILE study), Int. J. Cancer. 132 (4) (2013) 924–931.
[2] S.M.T. Wehrens, S. Christou, C. Isherwood, B. Middleton, M.A. Gibbs, S.N. Archer, et al., Meal timing regulates the human circadian system, Curr. Biol. 27 (12) (2017) 1768–1775.e3.
[3] H. Ogata, M. Horie, M. Kayaba, Y. Tanaka, A. Ando, I. Park, et al., Skipping breakfast for 6 days delayed the circadian rhythm of the body temperature without altering clock gene expression in human leukocytes, Nutrients 12 (9) (2020) 1–18.
[4] Y. Touitou, A. Bogdan, F. Lévi, M. Benavides, A. Auzéby, Disruption of the circadian patterns of serum cortisol in breast and ovarian cancer patients: relationships with tumour marker antigens, Br. J. Cancer 74 (8) (1996) 1248–1252.
[5] D.E. Blask, S.M. Hill, R.T. Dauchy, S. Xiang, L. Yuan, T. Duplessis, et al., Circadian regulation of molecular, dietary, and metabolic signaling mechanisms of human breast cancer growth by the nocturnal melatonin signal and the consequences of its disruption by light at night, J. Pineal Res. 51 (3) (2011) 259–269.
[6] J.A. Gwin, H.J. Leidy, A review of the evidence surrounding the effects of breakfast consumption on mechanisms of weight management, Adv. Nutr. 9 (6) (2018) 717–725.
[7] C. Gu, N. Brereton, A. Schweitzer, M. Cotter, D. Duan, E. Børsheim, et al., Metabolic effects of late dinner in healthy volunteers-a randomized crossover clinical trial, J. Clin. Endocrinol. Metab. 105 (8) (2020) 2789–2802.
[8] J.M. Kerver, E.J. Yang, S. Obayashi, L. Bianchi, W.O. Song, Meal and snack patterns are associated with dietary intake of energy and nutrients in US adults, J. Am. Diet Assoc. 106 (1) (2006) 46–53.
[9] C.R. Marinac, L. Natarajan, D.D. Sears, L.C. Gallo, S.J. Hartman, E. Arredondo, et al., Prolonged nightly fasting and breast cancer risk: findings from NHANES (2009-2010), Cancer Epidemiol. Biomarkers Prev. 24 (5) (2015) 783–789.
[10] C.R. Marinac, S.H. Nelson, C.I. Breen, S.J. Hartman, L. Natarajan, J.P. Pierce, et al., Prolonged nightly fasting and breast cancer prognosis, JAMA Oncol 2 (8) (2016) 1049–1055.
[11] G. Anderson, S. Cummings, L.S. Freedman, C. Furberg, M. Henderson, S.R. Johnson, et al., Design of the Women's Health Initiative clinical trial and observational study. The Women's Health Initiative Study Group, Control Clin. Trials 19 (1) (1998) 61–109.
[12] R.D. Langer, E. White, C.E. Lewis, J.M. Kotchen, S.L. Hendrix, M. Trevisan, The Women's Health Initiative Observational Study: baseline characteristics of participants and reliability of baseline measures, Ann. Epidemiol. 13 (9 Suppl) (2003) S107–S121.
[13] J. Hays, J.R. Hunt, F.A. Hubbell, G.L. Anderson, M. Limacher, C. Allen, et al., The Women's Health Initiative recruitment methods and results, Ann. Epidemiol. 13 (9 Suppl) (2003) S18–S77.
[14] P. Hayati Rezvan, K.J. Lee, J.A. Simpson, The rise of multiple imputation: a review of the reporting and implementation of the method in medical research, BMC Med. Res. Methodol. 15 (1) (2015) 30.
[15] M.A. Hernán, S. Hernández-Díaz, J.M. Robins, A structural approach to selection bias, Epidemiology 15 (5) (2004) 615–625.
[16] R.E. Patterson, A.R. Kristal, L.F. Tinker, R.A. Carter, M.P. Bolton, T. Agurs-Collins, Measurement characteristics of the Women's Health Initiative Food Frequency Questionnaire, Ann. Epidemiol. 9 (3) (1999) 178–187.
[17] M. Johnson-Kozlow, C.L. Rock, E.A. Gilpin, K.A. Hollenbach, J.P. Pierce, Validation of the WHI brief physical activity questionnaire among women diagnosed with breast cancer, Am. J. Health Behav. 31 (2) (2007) 193–202.
[18] SEER Extent of Disease Coding/SEER Training [Internet]. [cited 2022 May 5]. Available from: https://training.seer.cancer.gov/staging/systems/eod.html.
[19] A. George, S.R. Sturgeon, S.E. Hankinson, A.H. Shadyab, R.B. Wallace, K.W. Reeves, Psychotropic medication use and postmenopausal breast cancer risk, Cancer Epidemiol. Biomarkers Prev. 29 (1) (2020) 254–256.
[20] E.L. Busch, E.A. Whitsel, C.H. Kroenke, Y.C. Yang, Social relationships, inflammation markers, and breast cancer incidence in the Women's Health Initiative, Breast 39 (2018) 63.
[21] J.D. Curb, A. Mctiernan, S.R. Heckbert, C. Kooperberg, J. Stanford, M. Nevitt, et al., Outcomes ascertainment and adjudication methods in the Women's Health Initiative, Ann. Epidemiol. 13 (9) (2003) S122–S128.
[22] S.E. Chiuve, T.T. Fung, E.B. Rimm, F.B. Hu, M.L. McCullough, M. Wang, et al., Alternative dietary indices both strongly predict risk of chronic disease, J. Nutr. 142 (6) (2012) 1009–1018.
[23] L.L. Fajardo, M. Saint-Germain, T.J. Meakem, C. Rose, B.J. Hillman, Factors influencing women to undergo screening mammography, Radiology 184 (1) (1992) 59–63.
[24] W. Rakowski, M.A. Clark, R. Truchil, K. Schneider, S. Meersman, Smoking status and mammography among women aged 50–75 in the 2002 behavioral risk factor surveillance system, Women Health 41 (4) (2005) 1–21.
[25] K. Kerlikowske, Epidemiology of ductal carcinoma in situ, J. Natl. Cancer Inst. Monogr. 41 (2010) 139–141, 2010.
[26] J. Jin, Breast cancer screening guidelines in the United States, JAMA 314 (15) (2015) 1658.
[27] E. Banks, G. Reeves, V. Beral, D. Bull, B. Crossley, M. Simmonds, et al., Influence of personal characteristics of individual women on sensitivity and specificity of mammography in the Million Women Study: cohort study, BMJ 329 (7464) (2004) 477.
[28] G.K. Reeves, K. Pirie, J. Green, D. Bull, V. Beral, Million Women Study Collaborators, Comparison of the effects of genetic and environmental risk factors on in situ and invasive ductal breast cancer, Int. J. Cancer 131 (4) (2012) 930–937.
[29] B. Srour, S. Plancoulaine, V.A. Andreeva, P. Fassier, C. Julia, P. Galan, et al., Circadian nutritional behaviours and cancer risk: new insights from the NutriNet-santé prospective cohort study: Disclaimers, Int. J. Cancer 143 (10) (2018) 2369–2379.
[30] J.C. De Beer, L. Liebenberg, Does cancer risk increase with HbA1c, independent of diabetes? Br. J. Cancer 110 (9) (2014) 2361–2368.
[31] C. Hope, A. Robertshaw, K.L. Cheung, I. Idris, E. English, Relationship between HbA1c and cancer in people with or without diabetes: a systematic review, Diabet. Med. 33 (8) (2016) 1013–1025.