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Prospective Study of Avocado Consumption and Cancer Risk in US Men and Women

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Abstract

Avocados contain nutrients and phytochemicals that make it promising for cancer prevention, and chemopreventive properties have been demonstrated in prior studies. Prospective studies on avocado consumption and cancer risk have yet to be conducted. This study included data from 45,289 men in the Health Professionals Follow-Up Study (HPFS, 1986–2016) and 67,039 women in the Nurses' Health Study (NHS, 1986–2014). Avocado consumption was assessed using validated food frequency questionnaires every four years. Cox proportional hazards models calculated multivariable hazard ratios (HR) and 95% confidence intervals (CI) for associations between avocado consumption and risk of total and site-specific cancers in each cohort. In HPFS, consumption of ≥1 weekly serving of avocados was associated with decreased risk of total (HR 0.85; 95% CI 0.80–0.91), colorectal (HR 0.71; 95% CI 0.59–0.85), lung (HR 0.71; 95% CI 0.57–0.90), and bladder cancer (HR 0.72; 95% CI 0.57–0.90). In NHS, avocado consumption was associated with increased risk of breast cancer (HR 1.21; 95% CI 1.07–1.37). No associations were observed between avocado consumption and risk of total cancer (HR 1.06; 95% CI 0.98–1.14) or other site-specific cancers in NHS. Considering the surprising breast cancer finding, analyses were repeated using data from 93,230 younger women in the parallel NHSII (1991–2017). In NHSII, avocado consumption was not associated with breast cancer risk (HR 0.93, 95% CI 0.76–1.13). Overall, avocado consumption may be associated with reduced risk of total and some site-specific cancers in men. The positive association with breast cancer risk in NHS was not seen in the younger NHSII.

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Introduction

Cancer is an enormous public health issue, with 17 million incident cases and 9.5 million cancer deaths in 2018 globally.[1] It is the second leading cause of death worldwide, and cancer incidence and mortality are projected to increase in coming years.[1] The identification of modifiable factors for cancer prevention hold promise to reduce morbidity and mortality. Diets rich in fruits and vegetables are associated with a lower risk of several cancers and also contribute to reducing obesity, which itself is a major risk factor for cancer.[2,3]

Avocados are nutrient-dense fruits.[4,5] According to a study in the National Health and Nutrition Examination Survey, avocado consumers typically consume about one-half an avocado per day,[6] providing about 6.7 g of monounsaturated fatty acids, 4.6 g of dietary fiber, 345 mg of potassium, and 1.3 mg of vitamin E.[7] Avocado is also an abundant source of phytochemicals such as carotenoids, especially lutein.[4,7]

Several preliminary studies suggest that the phytochemicals present in avocados may be beneficial for cancer prevention. For example, phytochemicals and extracts from avocados exert anticarcinogenic effects in cancer cell lines, including apoptosis, cell cycle arrest, antioxidant activity, and inhibition of cell proliferation.[4,8,9] Avocados are rich in carotenoids, and epidemiologic studies have observed inverse associations between total circulating carotenoids and risk of bladder cancer[10] and breast cancer,[11] and between intake of certain carotenoids and risk of colorectal adenoma[12] and prostate cancer.[13]

The high level of monounsaturated fats in avocados is also relevant for cancer prevention. Studies have found monounsaturated fats to be inversely related to risk of oral and pharyngeal cancers,[14] pancreatic cancer,[15] and bladder cancer.[16] In fact, a case-control study in Jamaica found that increased intake of monounsaturated fats, mainly from avocados, was associated with reduced risk of prostate cancer.[17] These studies suggest that as a source of monounsaturated fats, avocados could be advantageous for cancer prevention.

While this evidence indicates the potential of avocados for cancer prevention, there is a lack of prospective epidemiology studies on avocado and cancer. Given their diverse phytochemicals and nutrients, we hypothesized that higher consumption of avocados would be associated with a lower risk of cancer overall, as well as a lower risk of site-specific cancers. In this study, we examined avocado consumption and risk of total and site-specific cancer in two large prospective cohort studies of US men and women followed for 30 years.

Methods

Study population

We leveraged data from two cohort studies: Health Professionals Follow-Up Study (HPFS) and Nurses' Health Study (NHS). These cohorts were created with the goal of studying risk factors for chronic illnesses such as cancer and heart disease. HPFS enrolled 51,529 male health professionals aged 40 to 70 in 1986, and NHS enrolled 121,700 female registered nurses aged 30 to 55 in 1976. Validated food frequency questionnaires (FFQs) were mailed to participants every four years to assess dietary intake, including avocado

consumption. Participants also completed questionnaires at baseline and every two years, providing information on demographics, lifestyle factors, and disease outcomes which were updated over follow-up. Both cohorts have over 30 years of follow-up with follow-up rates of 96% for cancer incidence and 99% for mortality.

This analysis included participants who completed an FFQ in 1986: baseline in HPFS and for NHS, the first questionnaire on which avocado consumption was asked. We excluded participants who had been diagnosed with any cancer aside from nonmelanoma skin cancer prior to 1986, who died prior to 1986 (NHS only), were missing data related to avocado consumption, or had implausible total energy intake (<500 or >3500 kcal/d for NHS, and <800 or >4200 kcal/d for HPFS). These exclusions left 45,289 men from HPFS and 67,039 women from NHS remaining to be used in this analysis.

Study protocol was approved by the institutional review boards of the Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health, and those of participating registries as required. Return of self-administered questionnaires implied written informed consent. This study was conducted in accordance with the U.S. Common Rule.

Assessment of avocado consumption

On FFQs, participants reported their average avocado consumption over the past year into one of the following categories: never, less than once per month, 1–3 times per month, once per week, 2–4 times per week, 5–6 times per week, once per day, or twice or more per day. One serving was defined as a half-fruit or half-cup of avocado. Previous studies have demonstrated the validity and reproducibility of FFQs for a range of foods and nutrients.[18,19]

Outcome assessment

In HPFS and NHS, cancer diagnoses are initially self-reported on biennial questionnaires, and then we seek permission from participants to retrieve medical records and pathology reports. Only cases confirmed by medical records were included in this analysis (~90% of reported cases). These documents were reviewed by study researchers to confirm the diagnosis and obtain information on the stage, anatomic location, and histology of the cancer. For this study, we looked at cancers of the: colon/rectum, lung, bladder, prostate (aggressive, men only), breast (women only), ovary (women only), and endometrium (women only), as well as melanoma and non-Hodgkin lymphoma.

Deaths were identified through the National Death Index and reports from next-of-kin and postal authorities. Follow-up was through January 2016 for HPFS and June 2014 for NHS.

Statistical analysis

Person-time of follow-up was calculated from the date of return of the 1986 questionnaire to the date of cancer diagnosis, death, or the end of follow-up, whichever came first. Participants' avocado consumption at each time point was collapsed into three categories: <1 serving per month, 1–3 servings per month, and ≥1 serving per week. Results from the

last two food frequency questionnaires were averaged to generate an estimate of avocado consumption across time.

Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between avocado intake and incidence of total and site-specific cancers. Covariate data were obtained from FFQs and biennial questionnaires over follow-up, and we used cumulative average updating for time-varying exposures. In multivariable models, we adjusted for age (continuous), race (white or non-white), height (quintiles), smoking history (never, former, current 1–14 cigarettes per day, current 15+ cigarettes per day), pack-years of smoking (0, 0.1–4.9, 5–19.9, 20–39.9, 40+ pack-years), family history of cancer (yes or no), multivitamin use (yes or no), alcohol intake (grams per day, quintiles), physical activity (Met-hours, quintiles), aspirin use (yes or no), body mass index (BMI, quintiles), total energy intake (quintiles), Alternate Healthy Eating Index 2010 (excluding avocados; quintiles), colonoscopy or sigmoidoscopy in the last two years (yes or no), and physical exam with a clinician in the last two years (yes or no). We additionally adjusted for prostate specific antigen testing in the past two years (yes or no) for men in HPFS, and for mammography (yes or no) and postmenopausal hormone use (pre-menopausal, never, former, current) for women in NHS. For breast cancer, we additionally adjusted for age at menarche (<12, 12–13, >13), oral contraceptive use (former, never), breastfeeding (never, < 6 months, 7+ months), BMI at age 18 (<20, 20–21.9, 22–23.9, 24+ kg/m^2), age at menopause (<46, 46–49.9, 50–51.9, 52+), and parity (none, 1, 2, 3+ children).

We also stratified by current age (<65 vs. ≥65 years), body mass index (BMI, <25 kg/m^2 vs. ≥25 kg/m^2), and Alternate Healthy Eating Index 2010 (above and below the median value) as a marker of healthier diet patterns. We stratified by these factors because they have been shown to be effect modifiers in other studies of diet and cancer.[20,21]

In sensitivity analyses, we excluded current smokers to examine the association between avocado intake and cancer risk unconfounded by current smoking. Finally, we performed additional breast cancer analyses examining associations between avocado consumption and breast cancer molecular subtypes including ER and PR status and stratified by diabetes, menopausal status at diagnosis, and mammogram history. All analyses were performed using SAS version 9.4 (RRID: SCR_008567; SAS Institute Inc).

Data availability

Information regarding procedures for obtaining and accessing HPFS data is described at https://sites.sph.harvard.edu/hpfs/for-collaborators/.

Results

Table 1 shows the characteristics of study participants in HPFS and NHS. Regular avocado consumption was relatively low in both cohorts, with only 16% of HPFS and 5% of NHS participants consuming at least one weekly serving over follow-up. Participants who consumed one or more servings of avocado per week tended to be more physically active, have a higher total energy intake, and have a better overall diet (AHEI). Participants in

this category also tended to have slightly lower BMI and consumed more fruits, vegetables, and alcohol. Differences across categories were not very large, indicating that no specific covariates were particularly strong confounders.

Avocado consumption was consistently higher in HPFS than NHS, with 29% of participants consuming at least one monthly serving in HPFS, compared to 17% in NHS in 1986. Avocado consumption increased steadily over time to 45% of HPFS and 26% of NHS participants consuming at least one monthly serving in 2010.

Over 30 years of follow-up, we identified 8,812 and 13,095 incident cancer cases in men and women, respectively. Table 2 shows the multivariable-adjusted associations between avocado consumption and total and site-specific cancer in HPFS and NHS. In HPFS, men who consumed one or more weekly servings of avocado had a 15% lower risk of total cancer compared to those who consumed less than one serving per month (95% CI 0.80–0.91). Men who consumed at least one weekly serving of avocado also had significantly decreased risk of colorectal cancer (HR 0.71; 95% CI 0.59–0.85), lung cancer (HR 0.71; 95% CI 0.57–0.90), and bladder cancer (HR 0.72; 95% CI 0.57–0.90). These findings remained when excluding current smokers (Supplementary Table S1). No significant associations were observed for melanoma, non-Hodgkin lymphoma, or aggressive prostate cancer (Table 2).

In NHS, no association was observed between avocado consumption and total cancer risk (HR 1.06; 95% CI 0.98–1.14) (Table 2). For site-specific cancers, women who consumed one or more servings per week had 21% increased risk of breast cancer compared to those who consumed less than one serving per month (95% CI 1.07–1.37). There were no significant associations for any other sites.

These findings remained in a sensitivity analysis excluding current smokers (Supplementary Table S1). Avocado consumption was associated with an increased risk of ER-negative breast cancer (HR 1.52; 95% CI 1.13–2.04), and modestly associated with PR-positive (HR 1.12; 95% CI 0.96–1.32), PR-negative (HR 1.33; 95% CI 1.06–1.67), and ER-positive (HR 1.14; 95% CI 0.99–1.32) disease (Table 3).

Next, to explore potential bias in our results on breast cancer, we stratified results in NHS for diabetes, menopause, and mammogram screening (Table 3). The positive association with avocado consumption and risk of breast cancer remained among post-menopausal women (HR 1.22; 95% CI 1.07–1.39) and women without diabetes (HR 1.21; 95% CI 1.06–1.37). There was no association among women with diabetes (HR 1.00; 95% CI 0.51–1.97), while results generated wide confidence intervals among pre-menopausal women (HR 1.19; 95% CI 0.68–2.07). There was also a significant positive association for both women who underwent a mammogram screening in the past two years (HR 1.14; CI 0.99–1.31), and for those without a recent mammogram (HR 1.43; CI 1.10–1.87).

Given the unexpected positive association of avocado consumption and breast cancer risk, we undertook a separate analysis within the parallel Nurses' Health Study II (NHSII). NHSII is similar to NHS[22] except that it is a younger cohort: the mean age of the NHSII study population was 36.6 years. Due to the age of the cohort at baseline and follow-up to date, we are only reasonably powered to look at breast cancer incidence separately in NHSII.

NHSII enrolled 116,430 women aged 25 to 42 in 1989. As in HPFS and NHS, NHSII questionnaires on demographics, lifestyle factors, and disease outcomes were completed at baseline and every two years over follow-up, and FFQs assessing dietary intake (including avocado intake) were completed every four years over follow-up, beginning in 1991. Like HPFS and NHS, the follow-up rate in NHSII exceeds 90%, with nearly complete ascertainment of cancer incidence (95%) and mortality (98%). Follow-up in the NHSII was through June 2017.

As in the NHS analyses, for NHSII, we excluded women who had been diagnosed with any cancer aside from nonmelanoma skin cancer prior to 1991, who died prior to 1991, were missing data related to avocado consumption, or had implausible total energy intake. These exclusions left 93,230 women to be included in the breast cancer analysis.

With 3,882 total breast cancers, we found no association between avocado consumption and breast cancer risk for the cumulative average (HR 0.93; 95% CI 0.76–1.13) or simple update (HR 1.00; 95% CI 0.81–1.23) models. Moreover, among postmenopausal women in NHSII (2,187 breast cancer cases), higher avocado consumption was not associated with a higher risk of breast cancer [HR Q5 vs. Q1 1.04 (95% CI 0.90, 1.21) p-trend=0.47].

Supplementary Table S2 shows the multivariable-adjusted associations for total cancer after stratifying by age, BMI, and AHEI. In HPFS, avocado consumption was associated with significantly lower risk of total cancer across all subgroups. In NHS, avocado consumption was not significantly associated with total cancer in any subgroup except for women aged 65 or older (HR 1.10; 95% CI 1.00–1.20) and those with higher scores of AHEI (HR 1.10; 95% CI 0.99–1.21). Avocado consumption was not associated with total cancer for women under age 65 (HR 0.97; 95% CI 0.85–1.12).

Discussion

In this large prospective analysis, avocado consumption was associated with significantly decreased risk of total cancer in men, while no association was observed for total cancer in women. Avocado consumption was also inversely associated with colorectal, lung, and bladder cancer in men, and, unexpectedly, positively associated with breast cancer among women in one of two cohorts.

Previous *in vitro* studies have demonstrated anticarcinogenic properties of avocados, suggesting their potential to reduce cancer risk.[8,23,24] Some studies suggest that monounsaturated fats, which exist in high levels in avocados, may have a protective effect against cancer at some sites.[14,15,25,26] Studies performed in rats also indicate the anti-inflammatory effects of avocados.[4,7,27]

These results align with the inverse association we observed between avocado consumption and total cancer risk for men in HPFS. In contrast, no association for total cancer was observed among women in NHS. This finding may be attributed to the lower intake in NHS, as only 5% of NHS participants consumed at least one weekly serving of avocado, compared to 16% in HPFS. Moreover, given that breast cancer is the most common malignancy in the NHS cohort, total cancer findings may be driven in great part by the positive association

for breast cancer. Future research should examine avocado consumption and cancer risk in populations with higher intake.

For site-specific cancers, the inverse association between avocado consumption and colorectal cancer risk in HPFS aligned with our hypothesis. Colorectal cancer risk is strongly associated with diet,[3,28] and previous studies demonstrated the anticarcinogenic properties of avocado extracts in colon cancer cell lines *in vitro*.[24]

In addition, we observed inverse associations of avocado consumption with lung and bladder cancer in men. Prior studies have observed that fruit consumption is inversely related to lung cancer risk,[29–32] and some have observed an inverse association in bladder cancer, though one study found this association was only significant in women.[33,34] While this relationship requires further investigation, it has been suggested that the fiber, vitamins, minerals, and phytochemicals provided by fruits may have anticarcinogenic properties.[2,3] Nevertheless, *in vitro* studies have not examined avocado consumption and lung or bladder cancer risk extensively. Future studies should further examine the relationship between avocado intake and risk of lung and bladder cancer.

Contrary to much of the literature, we observed no association between avocado consumption and risk of aggressive prostate cancer. Previous studies have found avocado extracts to have anticarcinogenic activity in prostate cancer cell lines.[8,35] Moreover, a case-control study found that monounsaturated fat intake, mainly from avocados, was associated with decreased risk of prostate cancer.[17] The discrepancy between our findings and those of prior studies may be attributed to the fact that we considered aggressive prostate cancer, rather than total prostate cancer. Additionally, case-control studies are more susceptible to biases than prospective cohort studies. In fact, when examining the relationship between vegetable fat and advanced prostate cancer, one case-control study observed an inverse association,[36] while a prospective cohort study observed no association,[37] as in our study on avocado intake.

Unexpectedly, we observed a positive association between avocado consumption and breast cancer risk, which remained after adjusting for several established breast cancer confounders and stratifying by potential effect modifiers. Previous studies found avocado extract to have anticancer effects in breast cancer cell lines.[23,24] Moreover, while no clinical studies have examined avocado consumption and breast cancer risk to our knowledge, studies have investigated breast cancer and carotenoids and monounsaturated fats. For example, a nested case-control study in the Nurses' Health Study found circulating total carotenoids to be inversely associated with breast cancer risk, especially among women of high mammographic density.[38] Additionally, some studies have found monounsaturated fat intake to be inversely associated with breast cancer risk,[25,26] while others have observed no association.[39–42] Considering these prior studies, we believe the positive association with avocados should be interpreted with caution and could be due to confounding by other factors, such as interactions with the healthcare system. Additionally, in NHSII, no association was observed between avocado consumption and breast cancer, both overall and among postmenopausal women. This result suggests that the surprising findings in NHS could be due to random chance.

Our study has several strengths. This is the first prospective epidemiological study to examine avocado consumption and cancer risk, to our knowledge. It was conducted in well-established cohorts with a large number of cancer cases. This study also included almost 30 years of follow-up with repeated dietary assessment and assessment of covariates.

This study has several limitations. Although we adjusted for a variety of cancer risk factors, there is still a possibility of residual confounding. Moreover, the cohorts are composed of primarily white participants, and should be repeated in a more racially diverse population. Finally, while large prospective cohorts were used in this study, only 28% of study participants consumed avocados regularly, resulting in a small sample size for the highest category of avocado consumption, particularly in NHS.

Overall, we found avocado consumption to be associated with decreased risk of total cancer among men, but not among women. Further prospective studies should be conducted to explore this relationship, particularly for breast cancer in women and lung and bladder cancer in men.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Prevention Relevance Statement

The results of this prospective study suggest that avocado consumption may be associated with decreased risk of total and some site-specific cancers in men.

Table 1.

Participant characteristics by avocado consumption in the Health Professionals Follow-Up Study (1986–2016) and Nurses' Health Study (1986–2014).

	Health Professionals Follow-Up Study			Nurses' Health Study		
	<1/month (PY=634,588)	**1–3/month (PY=236,610)**	**≥1/week (PY=168,782)**	**<1/month (PY=1,033,782)**	**1–3/month (PY=189,284)**	**≥1/week (PY=66,804)**
Age, years	64.4 (11.3)	62.5 (11.2)	62.6 (11.2)	62.6 (10.3)	63.7 (9.8)	65.9 (9.8)
White, %	95.2	94.5	94.7	98.4	96.9	96.9
Height, inches	70.1 (3.2)	70.3 (3.6)	70.3 (3.2)	64.5 (2.4)	64.7 (2.5)	64.8 (2.5)
Ever smoker, %	53.9	52.7	50.4	53.2	54.7	53.6
Family history of cancer, %	36.5	38.6	39.2	39.3	38.7	38.1
Multivitamin use, %	50.7	54.0	56.6	54.5	58.0	57.7
Alcohol consumption, g/d	10.6 (14.9)	12.9 (15.6)	13.5 (15.8)	5.1 (8.7)	7.7 (10.5)	8.4 (11.2)
Physical activity, METs-h/week	30.8 (27.5)	33.6 (28.4)	36.6 (31.2)	16.2 (16.7)	18.7 (18.1)	20.2 (18.4)
Aspirin use, %	42.0	41.9	42.7	54.3	54.3	53.3
Body mass index, kg/m^2	26.2 (3.8)	26.0 (3.8)	25.8 (3.7)	25.9 (4.8)	25 (4.3)	24.7 (4.3)
Total energy intake, Kcal/day	1952 (557)	1994 (552)	2067 (556)	1696 (512)	1763 (526)	1857 (536)
AHEI-2010	46.7 (10.1)	49.2 (9.7)	51.8 (9.7)	46.8 (9.1)	50.2 (9.0)	51.8 (9.2)
Red meat, servings/d	1.1 (0.8)	1.1 (0.7)	1.0 (0.7)	0.9 (0.5)	0.8 (0.5)	0.8 (0.6)
Fruit, servings/d	1.5 (1.1)	1.6 (1.2)	1.9 (1.2)	1.6 (1.0)	1.7 (1.0)	1.9 (1.1)
Vegetables, servings/d	3.0 (1.6)	3.3 (1.6)	3.7 (1.8)	3.4 (1.6)	3.8 (1.7)	4.2 (1.8)
Nuts, servings/d	0.5 (0.5)	0.5 (0.5)	0.6 (0.5)	0.3 (0.3)	0.4 (0.4)	0.5 (0.4)
Colonoscopy or sigmoidoscopy, %	25.9	28.0	28.5	22.6	24.4	23.8
PSA screening in 1994, %	36.5	35.7	37.5	-	-	-
Mammogram, %	-	-	-	73.0	74.1	72.4
Postmenopausal hormone, %	-	-	-	31.1	40.6	40.5

All variables other than age are standardized to the age distribution of all participants. Values presented as mean (SD) for continuous variables. AHEI-2010 excludes avocados. PY: person years; MET, metabolic equivalent of task; AHEI, Alternate Healthy Eating Index; PSA, prostate-specific antigen.

Table 2.

Multivariable-adjusted associations of avocado consumption and cancer risk in the Health Professionals Follow-Up Study and Nurses' Health Study.

	Health Professionals Follow-Up Study				Nurses' Health Study			
	<1/month (PY=634,588)	**1–3/month (PY=236,610)**	**≥1/week (PY=168,782)**	**p_{trend}**	**<1/month (PY=1,033,782)**	**1–3/month (PY=189,284)**	**≥1/week (PY=66,804)**	**p_{trend}**
Total cancer								
Cases	5826	1842	1144		10296	2027	772	
HR (95% CI)	1.00 (ref)	0.96 (0.91, 1.01)	0.85 (0.80, 0.91)	<0.001	1.00 (ref)	1.03 (0.98, 1.08)	1.06 (0.98, 1.14)	0.08
Colorectal cancer								
Cases	838	268	137		1016	190	60	
HR (95% CI)	1.00 (ref)	0.97 (0.84, 1.11)	0.71 (0.59, 0.85)	0.001	1.00 (ref)	1.04 (0.89, 1.22)	0.92 (0.70, 1.20)	0.85
Lung cancer								
Cases	669	189	85		1117	210	85	
HR (95% CI)	1.00 (ref)	0.96 (0.82, 1.14)	0.71 (0.57, 0.90)	0.01	1.00 (ref)	1.03 (0.88, 1.20)	1.13 (0.90, 1.42)	0.32
Melanoma								
Cases	603	200	177		509	120	42	
HR (95% CI)	1.00 (ref)	0.90 (0.76, 1.05)	1.06 (0.89, 1.26)	0.86	1.00 (ref)	1.14 (0.93, 1.41)	1.06 (0.76, 1.47)	0.35
Bladder cancer								
Cases	594	170	93		240	51	17	
HR (95% CI)	1.00 (ref)	0.91 (0.76, 1.08)	0.72 (0.57, 0.90)	0.004	1.00 (ref)	1.06 (0.77, 1.45)	0.99 (0.60, 1.65)	0.87
Non-Hodgkin lymphoma								
Cases	471	160	113		609	121	38	
HR (95% CI)	1.00 (ref)	1.01 (0.84, 1.21)	0.99 (0.80, 1.22)	0.93	1.00 (ref)	1.04 (0.85, 1.28)	0.91 (0.65, 1.27)	0.85
Aggressive prostate cancer								
Cases	706	258	145					
HR (95% CI)	1.00 (ref)	1.13 (0.98, 1.31)	0.87 (0.73, 1.05)	0.51				
Breast cancer								
Cases					3531	719	294	
HR (95% CI)					1.00 (ref)	1.05 (0.97, 1.15)	1.21 (1.07, 1.37)	0.003
Endometrial cancer								
Cases					742	128	39	

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	Health Professionals Follow-Up Study				Nurses' Health Study			
	<1/month (PY=634,588)	**1–3/month (PY=236,610)**	**≥1/week (PY=168,782)**	**p_{trend}**	**<1/month (PY=1,033,782)**	**1–3/month (PY=189,284)**	**≥1/week (PY=66,804)**	**p_{trend}**
HR (95% CI)					1.00 (ref)	0.91 (0.75, 1.11)	0.76 (0.55, 1.06)	0.08
Ovarian cancer								
Cases					390	76	25	
HR (95% CI)					1.00 (ref)	1.07 (0.83, 1.38)	0.95 (0.62, 1.43)	0.93

All models adjusted for age (continuous), race (white, non-white), height (quintiles), smoking history (never, former, current 1–14, current 15+), pack-years of smoking (0, 0.1–4.9, 5–19.9, 20–39.9, 40+), family history of cancer (yes, no), multivitamin use (yes, no), alcohol intake (quintiles), physical activity (quintiles), aspirin use (yes, no), body mass index (quintiles), total energy intake (quintiles), Alternate Healthy Eating Index 2010 (excluding avocados; quintiles), colonoscopy or sigmoidoscopy (yes, no), physical exam (yes, no). Models in HPFS additionally adjusted for prostate specific antigen testing (yes, no). Models in NHS additionally adjusted for mammography (yes, no) and postmenopausal hormone use (pre-menopausal, never, former, current).

Table 3.

Associations between avocado consumption and breast cancer in the Nurses' Health Study.

	Cases	<1/month	1–3/month	≥1/week	P_{trend}
Total Breast Cancer	4544	1.00 (ref)	1.05 (0.97, 1.14)	1.20 (1.06, 1.36)	0.005
ER status					
ER positive	3392	1.00 (ref)	1.09 (0.99, 1.20)	1.14 (0.99, 1.32)	0.02
ER negative	734	1.00 (ref)	0.95 (0.77, 1.19)	1.52 (1.13, 2.04)	0.06
PR status					
PR positive	2790	1.00 (ref)	1.09 (0.99, 1.21)	1.12 (0.96, 1.32)	0.05
PR negative	1284	1.00 (ref)	1.00 (0.85, 1.18)	1.33 (1.06, 1.67)	0.06
Diabetes					
Yes	249	1.00 (ref)	1.29 (0.86, 1.95)	1.00 (0.51, 1.97)	0.50
No	4295	1.00 (ref)	1.04 (0.95, 1.13)	1.21 (1.06, 1.37)	0.008
Menopause					
Post-menopause	4056	1.00 (ref)	1.08 (0.99, 1.18)	1.22 (1.07, 1.39)	0.001
Pre-menopause	402	1.00 (ref)	1.12 (0.83, 1.52)	1.19 (0.68, 2.07)	0.36
Mammogram					
Yes	3552	1.00 (ref)	1.07 (0.97, 1.17)	1.14 (0.99, 1.31)	0.04
No	992	1.00 (ref)	1.00 (0.82, 1.21)	1.43 (1.10, 1.87)	0.05

All models adjusted for age, race, height, smoking history, pack-years of smoking, family history of cancer, multivitamin use, alcohol intake, physical activity, aspirin use, body mass index, total energy intake, Alternate Healthy Eating Index 2010 (excluding avocados), colonoscopy or sigmoidoscopy, physical exam, mammography postmenopausal hormone use, age at menarche, oral contraceptive use, breastfeeding, BMI at 18 years of age, age at menopause, and parity.