Pet Ownership and Cancer Risk in the Women's Health Initiative

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Abstract

Background: Pet ownership and cancer are both highly prevalent in the United States. Evidence suggests that associations may exist between this potentially modifiable factor and cancer prevention, though studies are sparse. The present report examined whether pet ownership (dog, cat, or bird) is associated with lower risk for total cancer and site-specific obesity-related cancers.

Methods: This was a prospective analysis of 123,560 participants (20,981 dog owners; 19,288 cat owners; 1,338 bird owners; and 81,953 non–pet owners) enrolled in the Women's Health Initiative observational study and clinical trials. Cox proportional hazards models were used to estimate HR and 95% confidence intervals for the

association between pet ownership and cancer, adjusted for potential confounders.

Results: There were no significant relationships between ownership of a dog, cat, or bird and incidence of cancer overall. When site-specific cancers were examined, no associations were observed after adjustment for multiple comparisons.

Conclusion: Pet ownership had no association with overall cancer incidence.

Impact: This is the first large epidemiologic study to date to explore relationships between pet ownership and cancer risk, as well as associated risks for individual cancer types. This study requires replication in other sizable, diverse cohorts. *Cancer Epidemiol Biomarkers Prev; 25(9); 1311–6. ©2016 AACR.*

Introduction

Cancer is among the leading causes of death in the United States (1). The incidence of cancer is linked to several modifiable behavioral and lifestyle risk factors such as obesity, physical inactivity, and sedentary behavior (2, 3). Furthermore, cancer has been positively associated with numerous environmental risk factors (4) and stress-related psychosocial factors (5). Efforts to identify other potentially modifiable factors that may be associated with lower cancer risk are warranted.

According to the 2015–2016 National Pet Owners Survey, 65% of U.S. households (79.7 million) own a pet (6). Given this estimate and the health benefits pets provide, the "One Health" agenda is advocating for an integration of human, animal, environmental, and ecosystem health (7). Several studies have shown that the presence of dogs and cats in households is associated with reductions in the risk of atopic diseases related to increased environmental exposure to endotoxins (8–10). Consequently, it has been suggested that dog and cat ownership may improve immune function and play a protective role in the carcinogenesis of cancer, particularly non-Hodgkin's lymphoma (11, 12). Despite this evidence, specific biological mechanisms linking pet ownership to cancer are lacking, and efforts to identify an association between pet ownership (dogs, cats, or birds) and cancer risk have been limited to case–control studies with mixed results (12–19). For example, Tranah and colleagues (13) demonstrated dog ownership and cat ownership at any time was associated with a lower risk of non-Hodgkin's lymphoma as compared with never owning a pet. Conversely, Laumbacher and colleagues (12) found that 69 breast cancer patients in Germany were significantly more likely to own dogs as compared with 1,320 age-matched controls. These findings, and the fact that pet ownership is a potentially modifiable exposure, support the need for further investigation of the relationship between pet ownership and cancer risk. The purpose of the present study was to expand upon existing evidence using findings from the well-characterized, diverse sample of over 160,000 postmenopausal women enrolled in the Women's Health Initiative (WHI) observational study and clinical trials (20, 21). The relationships between pet ownership and cancer risk were evaluated under the hypothesis that pet ownership compared with not owning a pet would be associated with lower risk for total cancer.

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Note: Trial Registration: ClinicalTrials.gov, NCT00000611

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Materials and Methods

Study design and sample

Between 1993 and 1998, the WHI recruited a large and diverse sample of postmenopausal women (50 to 79 years of age) to

participate in one or more clinical trials ($n = 68,132$) or an observational study ($n = 93,676$; ref. 20). Detailed information regarding the study design has been published elsewhere (20). In brief, the clinical trials included a randomized, placebo-controlled trial of hormone therapy (estrogen alone or estrogen plus progestin), a trial of calcium and vitamin D supplementation, and a low-fat diet modification trial. Women could enroll in one or more clinical trials if they met eligibility criteria. Women found to be ineligible, unwilling, or not interested in participating in a clinical trial were invited to participate in the observational study. All women provided written informed consent prior to enrollment, and study procedures were approved by the Institutional Review Boards of the 40 U.S. participating clinical centers. Women were excluded from the present analysis if information on pet ownership was missing ($n = 1,824$), if they owned multiple types of pets ($n = 11,540$), or had pets other than dogs, cats, or birds ($n = 7,048$). An additional 14,152 women with a personal history of cancer (or unknown personal history of cancer) were excluded, plus 546 with missing follow-up data regarding health status that would inform on any new cancer diagnosis. A further 2,708 and 430 women who had incident cancer or death, respectively, within the first 2 years of follow-up, were excluded. Thus, the final analytic cohort included 123,560 participants, of which 19,396 (15.7%) developed cancer during follow-up (mean follow-up time 11.0 ± 5.0 years; 1,362,658.1 person-years of follow-up).

Pet ownership

For the purpose of this analysis, women were identified as a pet owner if they selfreported at baseline that their current pet was a dog ($n = 20,981$), cat ($n = 19,288$), or bird ($n = 1,338$; ref. 22). Non-pet owners ($n = 81,953$) were participants who did not report owning pets of any type at baseline.

Ascertainment of cancer outcomes

Cancer outcome definitions, documentation, and classifications applied within the WHI have been published in detail (23). Briefly, participants selfreported whether they had been diagnosed with any clinical outcomes on a prespecified list, including any cancer, twice per year. In addition, enrolled women were expected to undergo cancer screenings including colonoscopies, pap smears, and mammograms. Self report of cancer was verified by medical record and pathology review by a centrally trained WHI physician adjudicator at each of the participating clinical centers (23). Central adjudication and coding were conducted using the NCI's Surveillance, Epidemiology, and End Results coding system (24). The current analysis includes solid tumor obesity-related cancers (invasive breast, colorectal, endometrial, kidney, bladder, stomach, lung, and ovarian) and lymphoma adjudicated through August 2014.

Covariates

Demographic information, personal habits, and psychosocial measures were collected at baseline using study-specific questionnaires (20). Available data included selfreported age, race/ethnicity, education (≤high school, some college, ≥college), neighborhood socioeconomic status (NSES; 0–100; higher scores indicating greater affluence), living alone status (no, yes), alcohol use (drinks/week), smoking pack-years (never smoker, <5, 5 to 19, and ≥20), hormone replacement therapy (HRT) use (never, former, current), and history of diabetes (no, yes). Depression

was measured by using participant responses to the Burmam 8-item scale (25). Values range from 0 to 1, with higher scores indicating greater depression symptomatology. A threshold of 0.06 represents women who experienced symptoms consistent with major depressive disorders (25). Social support was measured with 9 items from the Medical Outcomes Study Social Support Survey (26). Total scores are the sum of scores for the 9 items and range from 9 to 45. Additional exposures suggested to alter cancer diagnosis include overweight/obesity (27, 28), diet quality (29), and physical activity (30). Height, weight, and waist circumference (WC) were measured at baseline by certified staff using standardized procedures and instruments. Body mass index (BMI; kg/m^2) and WC were categorized according to standard cutoffs (31). Estimates of overall diet quality were calculated according the Healthy Eating Index (HEI)-2005 (32, 33). Physical activity was measured using a validated selfreported questionnaire (34, 35) and categorized *a priori* as ≥7.5 MET-hr/wk (consistent with current federal guidelines of 150 min/wk; refs. 36, 37).

Statistical analysis

Baseline characteristics were compared between pet owners (dog, cat, or bird) and non-pet owners using χ^2 tests for categorical variables or ANOVA for continuous variables. Cox proportional hazards models were used to estimate HR and 95% confidence intervals (CI) for the association between pet ownership and cancer, adjusted for potential confounders, identified as variables associated with both pet ownership and any cancer ($P < 0.10$). Thus, multivariate models were adjusted for age, race/ethnicity, NSES, education, BMI, WC, smoking, alcohol, HEI-2005, physical activity, HRT use, history of diabetes, living alone, and social support. Participants were censored at the time of last known contact or death; in the analysis of specific cancers, women were not censored at the occurrence of another cancer. Multiple comparisons were corrected using Bonferroni adjustment. Because there were nine cancer types tested, a P value had to be lower than 0.006 to be statistically significant for multiple comparisons adjustment. Specific to breast cancer models, women without a mammogram within 2 years before baseline were excluded. All analyses were conducted using Stata 14.1 (StataCorp).

Results

Baseline characteristics of study participants

The final analytical sample comprised 123,560 participants (20,981 dog owners; 19,288 cat owners; 1,338 bird owners; and 81,953 non-pet owners) with the majority reported to be non-Hispanic white and well educated (Table 1). Pet owners were generally younger, less likely to live alone, and reported higher HEI-2005 scores, less time engaging in physical activity, and more pack-years of smoking compared with non-pet owners. In addition, dog and bird owners had higher mean BMI than non-pet owners.

Pet ownership and cancer risk

In age-adjusted and multivariate models, there were no significant relationships between pet ownership (dog, cat, or bird) and incidence of cancer overall (Table 2). Cat ownership was associated with a 15% higher incidence of lung cancer in age-adjusted models (HR, 1.15; 95% CI, 1.02–1.29); this relationship was not statistically significant in the multivariate model after adjustment for multiple comparisons. However,

Table 1. Baseline characteristics of women according to pet ownership status: % or mean ± SD (WHI, United States, 1993–1998)

Characteristics[a]	No pets n = 81,953	Dog(s) only n = 20,981	Cat(s) only n = 19,288	Bird(s) only n = 1,338
Age (y)				
Mean ± SD	64.1 ± 7.1	61.7 ± 7.0	61.8 ± 7.1	62.3 ± 7.4
Race/ethnicity				
Non-Hispanic white	80.4	80.6	91.1	75.0
Black	11.4	8.69	3.66	6.28
Hispanic	3.72	5.35	2.29	11.7
Other/unknown	4.55	5.35	2.96	7.03
NSES	75.7 ± 8.8	75.4 ± 8.8	76.6 ± 7.8	73.8 ± 9.5
Education				
≤High school	23.6	23.2	17.7	32.8
Some college	36.9	40.4	36.8	37.4
≥College	39.5	36.5	45.6	29.7
BMI (kg/m^2)				
<25	36.0	32.6	37.2	32.0
25–29.9	35.1	34.9	33.9	34.1
≥30	28.9	32.6	28.9	33.8
Mean ± SD	27.8 ± 5.8	28.3 ± 6.0	27.8 ± 6.0	28.5 ± 6.1
WC (cm)				
≤88	61.8	58.7	61.5	56.9
>88	38.2	41.3	38.5	43.1
Mean ± SD	85.9 ± 13.6	87.1 ± 13.9	86.2 ± 14.1	87.6 ± 14.3
Smoking pack-years				
Never smoker	54.2	51.1	49.5	54.2
<5	14.3	14.6	15.0	14.6
5 to <20	14.1	15.0	14.9	12.8
≥20	17.4	19.4	20.6	18.4
Alcohol use (drink/wk)				
<1	62.7	64.1	58.1	68.2
1–7	25.9	24.6	28.5	22.6
≥7	11.3	11.2	13.4	9.28
HEI-2005	67.9 ± 10.6	66.2 ± 10.8	67.2 ± 10.7	66.9 ± 10.7
Physical activity (MET-hr/wk)				
<7.5	44.5	48.4	46.6	49.0
≥7.5	55.5	51.6	53.4	51.0
Mean ± SD	12.7 ± 13.8	11.8 ± 13.4	12.2 ± 13.5	12.0 ± 13.3
HRT use				
Never	45.1	40.6	41.2	46.3
Former	15.6	15.2	14.7	16.5
Current	39.3	44.3	44.1	37.3
History of diabetes				
No	95.7	95.4	96.3	94.0
Yes	4.26	4.59	3.69	5.98
Live alone				
No	67.6	78.3	69.2	71.0
Yes	32.4	21.7	30.8	29.0
Depression score				
<0.009	76.8	73.4	74.3	72.7
0.009–0.06	13.3	14.5	14.8	15.7
>0.06	9.93	12.1	11.0	11.6
Social support construct	36.1 ± 7.7	36.0 ± 7.7	35.8 ± 7.7	35.1 ± 8.2

[a]Missing data: NSES (n = 12,058; 9.8%), education (n = 907; 0.7%), BMI (n = 1059; 0.9%), WC (n = 444; 0.4%), smoking pack-years (n = 4,050; 3.3%), alcohol (n = 750; 0.6%), HEI-2005 (n = 3,719; 3.0%), physical activity (n = 5,599; 4.5%), HRT use (n = 112; 0.1%), history of diabetes (n = 99; 0.1%), live alone (n = 13,521; 11.0%), depression (n = 2,999; 2.4%), and social support (n = 2,805; 2.3%).

in a sensitivity analysis restricted to never-smokers (Table 3), the association between cat ownership and lung cancer was still in the positive direction (HR, 1.13; 95% CI, 0.80–1.59). In addition, cat ownership was associated with a 29% lower incidence of endometrial cancer (HR, 0.71; 95% CI, 0.52–0.95) compared with non-pet owners; however, this relationship was not statistically significant after adjustment for multiple comparisons. There were no significant associations between pet ownership (dog, cat, or bird) and overall cancer incidence or any other specific cancer types when stratifying by BMI, physical activity, or living alone (data not shown).

Discussion

The present study is the largest prospective study, to our knowledge, that explores pet ownership and cancer risk. Of the 123,560 postmenopausal women included in the analysis, 19,396 incident cancers were reported. Pet ownership (dog, cat, or bird) was not found to be associated with overall cancer risk and no associations with specific cancers existed after adjustment for multiple comparisons. Notably, pet owners were more sedentary, had a higher pack year smoking history, and had a higher BMI compared with non-pet owners.

Table 2. Associations between pet ownership and incident cancer (WHI, United States, 1993–1998)

	No pets		Dog(s) only		Cat(s) only		Bird(s) only	
	Events		Events		Events		Events	
Cancer type	*n* of 81,953 (%)	HR	*n* of 20,981 (%)	HR (95% CI)	*n* of 19,288 (%)	HR (95% CI)	*n* of 1,338 (%)	HR (95% CI)
Any	12,827 (15.7)		3,241 (15.5)		3,139 (16.3)		189 (14.1)	
Age-adjusted		1.00		1.03 (0.99–1.07)		1.04 (1.00–1.09)		0.96 (0.83–1.11)
Multivariate[a]		1.00		1.01 (0.96–1.06)		0.98 (0.93–1.03)		0.97 (0.81–1.15)
Breast[b]	3,525 (5.25)		905 (5.40)		890 (5.71)		46 (4.47)	
Age-adjusted		1.00		1.03 (0.96–1.11)		1.05 (0.98–1.13)		0.87 (0.65–1.16)
Multivariate[a]		1.00		1.00 (0.91–1.09)		0.98 (0.90–1.07)		0.98 (0.70–1.37)
Colorectal	1,256 (1.53)		308 (1.47)		278 (1.44)		21 (1.57)	
Age-adjusted		1.00		1.08 (0.95–1.22)		1.01 (0.89–1.15)		1.15 (0.75–1.77)
Multivariate[a]		1.00		1.03 (0.89–1.20)		0.88 (0.75–1.04)		0.84 (0.46–1.53)
Endometrial	734 (0.90)		167 (0.80)		190 (0.99)		12 (0.90)	
Age-adjusted		1.00		0.89 (0.75–1.05)		1.05 (0.90–1.24)		1.04 (0.59–1.84)
Multivariate[a]		1.00		0.97 (0.80–1.17)		0.88 (0.72–1.08)		1.14 (0.59–2.21)
Kidney	288 (0.35)		56 (0.27)		59 (0.31)		7 (0.52)	
Age-adjusted		1.00		0.79 (0.60–1.06)		0.87 (0.66–1.15)		1.60 (0.75–3.38)
Multivariate[a]		1.00		0.83 (0.59–1.16)		0.84 (0.60–1.17)		1.53 (0.63–3.73)
Bladder	356 (0.43)		84 (0.40)		93 (0.48)		3 (0.22)	
Age-adjusted		1.00		1.03 (0.81–1.31)		1.18 (0.94–1.48)		0.58 (0.19–1.81)
Multivariate[a]		1.00		0.88 (0.65–1.19)		1.18 (0.90–1.54)		0.86 (0.27–2.68)
Stomach	115 (0.14)		25 (0.12)		32 (0.17)		1 (0.07)	
Age-adjusted		1.00		0.98 (0.64–1.52)		1.31 (0.88–1.94)		n/a
Multivariate[a]		1.00		0.97 (0.58–1.63)		1.27 (0.79–2.05)		n/a
Lung	1,400 (1.71)		361 (1.72)		360 (1.87)		20 (1.49)	
Age-adjusted		1.00		1.11 (0.99–1.25)		1.15 (1.02–1.29)		0.98 (0.63–1.52)
Multivariate[a]		1.00		1.01 (0.87–1.16)		1.04 (0.91–1.20)		0.79 (0.44–1.44)
Ovary	474 (0.58)		116 (0.55)		116 (0.60)		8 (0.60)	
Age-adjusted		1.00		0.98 (0.80–1.20)		1.02 (0.83–1.25)		1.09 (0.54–2.19)
Multivariate[a]		1.00		1.08 (0.85–1.36)		1.02 (0.80–1.29)		1.20 (0.54–2.70)
Lymphoma	695 (0.85)		158 (0.75)		155 (0.80)		7 (0.52)	
Age-adjusted		1.00		0.96 (0.81–1.15)		0.98 (0.82–1.17)		0.68 (0.32–1.43)
Multivariate[a]		1.00		1.04 (0.85–1.28)		0.95 (0.78–1.17)		0.42 (0.14–1.31)

[a]Multivariate models adjusted for age, race/ethnicity, NSES, education, BMI, WC, smoking pack-years, alcohol drinks/wk, HEI-2005, physical activity, HRT use, history of diabetes, living alone, and social support.
[b]Invasive breast cancer, restricted to women who reported having a mammogram within 2 years before baseline; total sample sizes reduced as follows: no pets (*n* = 67,113), dog(s) only (*n* = 16,751), cat(s) only (*n* = 15,597), bird only (*n* = 1,028).

Our exploratory findings contribute to the limited literature on pet ownership and cancer risk. Tranah and colleagues (13) examined the relationship between dog and cat exposures and non-Hodgkin's lymphoma in a case–control study (1,591 cases, mean age 57 years; and 2,515 controls, mean age 54 years) of men and women in the U.S. Dog and cat ownership at any time as compared with those who never owned a pet was associated with a 21% lower risk of non-Hodgkin's lymphoma (OR, 0.79; 95% CI, 0.54–0.94). Longer duration of cat and dog ownership

was inversely associated with non-Hodgkin's lymphoma risk (*P* trend=0.008 and 0.04, respectively). Although we did not have specific information on non-Hodgkin's lymphoma, we found no evidence to support an association between pet ownership and lymphoma. Laumbacher and colleagues (12) compared the frequency of pet ownership in 69 breast cancer patients and 1,320 age-matched controls in women ages ≥ 30 years or more living in Germany. Breast cancer patients were interviewed about keeping household pets at the moment of seeking consultation for

Table 3. Associations between pet ownership and incident cancer, restricted to never smokers (WHI, United States, 1993–1998)

	No pets		Dog(s) only		Cat(s) only		Bird(s) only	
	Events		Events		Events		Events	
Cancer type	*n* of 30,833 (%)	HR	*n* of 7,456 (%)	HR (95% CI)[a]	*n* of 6,697 (%)	HR (95% CI)[a]	*n* of 488 (%)	HR (95% CI)[a]
Any	4,405 (14.3)	1.00	1,050 (14.1)	1.02 (0.95–1.09)	939 (14.0)	0.96 (0.89–1.03)	70 (14.3)	1.06 (0.84–1.34)
Breast[b]	1,305 (5.12)	1.00	317 (5.30)	1.02 (0.90–1.15)	273 (4.97)	0.91 (0.80–1.04)	17 (4.49)	0.89 (0.55–1.43)
Colorectal	451 (1.46)	1.00	109 (1.46)	1.10 (0.89–1.36)	80 (1.19)	0.87 (0.69–1.11)	8 (1.64)	1.18 (0.58–2.37)
Endometrial	311 (1.01)	1.00	62 (0.83)	0.81 (0.61–1.06)	52 (0.78)	0.71 (0.52–0.95)	8 (1.64)	1.67 (0.83–3.37)
Kidney	114 (0.37)	1.00	19 (0.25)	0.74 (0.45–1.20)	17 (0.25)	0.70 (0.42–1.17)	4 (0.82)	2.22 (0.81–6.03)
Bladder	88 (0.29)	1.00	18 (0.24)	0.90 (0.54–1.51)	28 (0.42)	1.49 (0.97–2.30)	1 (0.20)	0.75 (0.10–5.36)
Stomach	48 (0.16)	1.00	7 (0.09)	0.69 (0.31–1.54)	9 (0.13)	1.01 (0.49–2.07)	0 (0.00)	n/a
Lung	175 (0.57)	1.00	42 (0.56)	1.17 (0.83–1.65)	40 (0.60)	1.13 (0.80–1.59)	2 (0.41)	0.83 (0.21–3.36)
Ovary	174 (0.56)	1.00	41 (0.55)	1.01 (0.72–1.43)	45 (0.67)	1.16 (0.83–1.61)	3 (0.61)	1.17 (0.37–3.66)
Lymphoma	268 (0.87)	1.00	55 (0.74)	0.94 (0.70–1.26)	54 (0.81)	0.96 (0.72–1.29)	1 (0.20)	0.26 (0.04–1.85)

[a]Multivariate models adjusted for age, race/ethnicity, NSES, education, BMI, WC, smoking pack-years, alcohol drinks/wk, HEI-2005, physical activity, HRT use, history of diabetes, living alone, and social support.
[b]Invasive breast cancer, restricted to women who reported having a mammogram within 2 years before baseline; total sample sizes reduced as follows: no pets (*n* = 25,486), dog(s) only (*n* = 5,984), cat(s) only (*n* = 5,491), bird only (*n* = 379).

immunotherapy. Approximately 37.7% of breast cancer patients owned a dog at the time of consultation and throughout the previous 10 years compared with 14.8% in the age-matched control population (RR, 3.5; $P < 0.001$). There was no difference in cat ownership between the groups. Our data showed no evidence on an association between pet ownership and breast cancer risk regardless of the type of pet. Swensen and colleagues (14) demonstrated no association between exposure to pets (either any pet, dog, or cat) and the development of childhood leukemia (OR, 1.01; 95% CI, 0.89–1.20) in a case–control analysis (1,248 cases and 1,358 controls) of children in the United States and Canada. To our knowledge, the risk of developing other specific cancer types in dog and cat owners versus non-pet owners has not been examined previously.

Although the present study did not demonstrate a significant association between cat ownership and incident lung cancer after adjustment for multiple comparisons, associations between pet ownership and altered immune function and desensitization to allergens are well accepted (7). Specifically, exposure to allergens from dander within the household (e.g., bedding, furniture, carpets) could be inhaled into the lungs, inciting a subtle, chronic immune response that leads to chronic inflammation and eventual cell-cycle dysregulation (38). It is also possible that second-hand smoke exposure may be embedded in the fur and inhaled by its owner, promoting cell inflammation and lung tumorigenesis (39, 40). An exploratory analysis of current smokers in our study who owned either a dog or cat (or both) at baseline supports this hypothesis. Among current smokers, dog/cat ownership was associated with a 24% higher incidence of lung cancer in a multivariate model (HR, 1.24; 95% CI, 1.04–1.48). The most plausible explanation for this finding is that analytical adjustment may not be adequate given the strong association between smoking and lung cancer (41). These findings should be further evaluated to determine if they can be replicated in other cohorts.

Strengths and limitations

Our study's strengths lie in our study sample, which has well characterized demographic, lifestyle, and clinical variables, and detailed long term exposure data for a diverse, large sample of older women including information regarding pet ownership. However, even though follow-up time was long on average, it may not have been long enough to observe an association between pet ownership and overall cancer risk. Further, the duration of pet ownership was not collected in our study, including the history of pet ownership or the number of pets present in the household. Common behavioral patterns of pet owners, such as dog walking time and physical exertion, were not discretely measured, although we previously demonstrated that dog owners were more likely to walk $\geq$ 150 min/wk and be less sedentary than non-dog owners in the WHI (22). Moreover, there were only 20 cases of lung cancer among bird owners in the present study. Thus, there is limited power to evaluate associations between bird ownership and lung cancer risk. Finally, data for potential environmental mechanisms of carcinogenesis (e.g., occupational or home/outdoor endotoxin and pollutant exposure), immune status, or allergies of women that could have influenced our findings were not collected at baseline and therefore were not included in our investigation. Cat owners in particular may have an added environmental exposure related to the litter box particulates that could be explored in future investigations.

Conclusion

Pet ownership was not associated with overall cancer risk among postmenopausal women. To our knowledge, the current investigation, derived from the well-characterized WHI prospective study, is the first large epidemiologic study that has explored pet ownership and overall cancer risk, as well as associated risks for individual cancer types. This study contributes to the sparse existing literature on pet ownership and cancer risk and raises the need for future analysis of other sizable, diverse cohorts. Future research should consider collection of environmental exposures that may differ for individuals with or without various pets.

Disclosure of Potential Conflicts of Interest

R.T. Chlebowski is an advisor at Genomic Health and is a consultant/advisory board member for Genentech, Genomic Health, Novartis, and Pfizer. No potential conflicts of interest were disclosed by the other authors.

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References

1. Minino AM. Death in the United States, 2011. NCHS Data Brief 2013:1–8.
2. Schottenfeld D, Beebe-Dimmer JL, Buffler PA, Omenn GS. Current perspective on the global and United States cancer burden attributable to lifestyle and environmental risk factors. Annu Rev Public Health 2013; 34:97–117.
3. Spring B, Ockene JK, Gidding SS, Mozaffarian D, Moore S, Rosal MC, et al. Better population health through behavior change in adults: A call to action. Circulation 2013;128:2169–76.
4. Danaei G, Vander Hoorn S, Lopez AD, Murray CJ, Ezzati M. Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. Lancet (London, England) 2005;366:1784–93.
5. Mehnert A, Koch U. Psychological comorbidity and health-related quality of life and its association with awareness, utilization, and need for psychosocial support in a cancer register-based sample of long-term breast cancer survivors. J Psychosom Res 2008;64:383–91.
6. American Pet Products Association. 2015–2016 APPA National Pet Owners Survey. American Pet Products Association: Greenwich, CT;2015.
7. Takashima GK, Day MJ. Setting the One Health agenda and the human-companion animal bond. Int J Environ Res Public Health 2014;11: 11110–20.
8. Ownby DR, Peterson EL, Wegienka G, Woodcroft KJ, Nicholas C, Zoratti E, et al. Are cats and dogs the major source of endotoxin in homes? Indoor Air 2013;23:219–26.
9. Ownby DR, Johnson CC, Peterson EL. Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6 to 7 years of age. JAMA 2002;288:963–72.
10. Konradsen JR, Fujisawa T, van Hage M, Hedlin G, Hilger C, Kleine-Tebbe J, et al. Allergy to furry animals: New insights, diagnostic approaches, and challenges. J Allergy Clin Immunol 2015;135:616–25.
11. Gern JE, Reardon CL, Hoffjan S, Nicolae D, Li Z, Roberg KA, et al. Effects of dog ownership and genotype on immune development and atopy in infancy. J Allergy Clin Immunol 2004;113:307–14.
12. Laumbacher B, Fellerhoff B, Herzberger B, Wank R. Do dogs harbour risk factors for human breast cancer? Med Hypotheses 2006;67:21–6.
13. Tranah GJ, Bracci PM, Holly EA. Domestic and farm-animal exposures and risk of non-Hodgkin's lymphoma in a population-based study in the San Francisco Bay Area. Cancer Epidemiol Biomarkers Prev 2008;17:2382–7.
14. Swensen AR, Ross JA, Shu XO, Reaman GH, Steinbuch M, Robison LL. Pet ownership and childhood acute leukemia (USA and Canada). Cancer Causes Control 2001;12:301–3.
15. Holst PA, Kromhout D, Brand R. For debate: Pet birds as an independent risk factor for lung cancer. BMJ 1988;297:1319–21.
16. Gardiner AJ, Forey BA, Lee PN. Avian exposure and bronchogenic carcinoma. BMJ 1992;305:989–92.
17. Kohlmeier L, Arminger G, Bartolomeycik S, Bellach B, Rehm J, Thamm M. Pet birds as an independent risk factor for lung cancer: Case-control study. BMJ 1992;305:986–9.
18. Freeman LEB, DeRoos AJ, Koutros S, Blair A, Ward MH, Alavanja M, et al. Poultry and livestock exposure and cancer risk among farmers in the agricultural health study. Cancer Causes Control 2012;23:663–70.
19. Alavanja MC, Brownson RC, Berger E, Lubin J, Modigh C. Avian exposure and risk of lung cancer in women in Missouri: Population based case-control study. BMJ 1996;313:1233–5.
20. Design of the Women's Health Initiative clinical trial and observational study. The Women's Health Initiative Study Group. Control Clin Trials 1998;19:61–109.
21. Hays J, Hunt JR, Hubbell FA, Anderson GL, Limacher M, Allen C, et al. The Women's Health Initiative recruitment methods and results. Ann Epidemiol 2003;13:S18–77.
22. Garcia DO, Wertheim BC, Manson JE, Chlebowski RT, Volpe SL, Howard BV, et al. Relationships between dog ownership and physical activity in postmenopausal women. Prev Med 2015;70:33–8.
23. Curb JD, McTiernan A, Heckbert SR, Kooperberg C, Stanford J, Nevitt M, et al. Outcomes ascertainment and adjudication methods in the Women's Health Initiative. Ann Epidemiol 2003;13:S122–8.
24. Beresford SA, Johnson KC, Ritenbaugh C, Lasser NL, Snetselaar LG, Black HR, et al. Low-fat dietary pattern and risk of colorectal cancer: The Women's Health Initiative Randomized Controlled Dietary Modification Trial. JAMA 2006;295:643–54.
25. Burnam MA, Wells KB, Leake B, Landsverk J. Development of a brief screening instrument for detecting depressive disorders. Med Care 1988;26:775–89.
26. Sherbourne CD, Stewart AL. The MOS social support survey. Soc Sci Med 1991;32:705–14.
27. Vucenik I, Stains JP. Obesity and cancer risk: Evidence, mechanisms, and recommendations. Ann N Y Acad Sci 2012;1271:37–43.
28. Neuhouser ML, Aragaki AK, Prentice RL, Manson JE, Chlebowski R, Carty CL, et al. Overweight, obesity, and postmenopausal invasive breast cancer risk: A secondary analysis of the Women's Health Initiative Randomized Clinical Trials. JAMA Oncol 2015;1:611–21.
29. Arem H, Reedy J, Sampson J, Jiao L, Hollenbeck AR, Risch H, et al. The Healthy Eating Index 2005 and risk for pancreatic cancer in the NIH-AARP study. J Natl Cancer Inst 2013;105:1298–305.
30. McTiernan A, Kooperberg C, White E, Wilcox S, Coates R, Adams-Campbell LL, et al. Recreational physical activity and the risk of breast cancer in postmenopausal women: The Women's Health Initiative Cohort Study. JAMA 2003;290:1331–6.
31. NOEIE Panel. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults–the evidence report. National Institutes of Health. Obes Res 1998;6Suppl 2:51S–209S.
32. Guenther PM, Reedy J, Krebs-Smith SM. Development of the Healthy Eating Index-2005. J Am Diet Assoc 2008;108:1896–901.
33. Guenther PM, Reedy J, Krebs-Smith SM, Reeve BB. Evaluation of the Healthy Eating Index-2005. J Am Diet Assoc 2008;108:1854–64.
34. Pettee Gabriel K, McClain JJ, Lee CD, Swan PD, Alvar BA, Mitros MR, et al. Evaluation of physical activity measures used in middle-aged women. Med Sci Sports Exerc 2009;41:1403–12.
35. Meyer AM, Evenson KR, Morimoto L, Siscovick D, White E. Test-retest reliability of the Women's Health Initiative physical activity questionnaire. Med Sci Sports Exerc 2009;41:530–8.
36. Centers for Disease C, Prevention. Adult participation in aerobic and muscle-strengthening physical activities–United States, 2011. MMWR Morb Mortal Wkly Rep 2013;62:326–30.
37. Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, et al. Physical activity and public health in older adults: Recommendation from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc 2007;39:1435–45.
38. Ihre E, Zetterstrom O. Increase in non-specific bronchial responsiveness after repeated inhalation of low doses of allergen. Clin Exp Allergy 1993;23:298–305.
39. D'Anna C, Cigna D, Costanzo G, Ferraro M, Siena L, Vitulo P, et al. Cigarette smoke alters cell cycle and induces inflammation in lung fibroblasts. Life Sci 2015;126:10–8.
40. Takahashi H, Ogata H, Nishigaki R, Broide DH, Karin M. Tobacco smoke promotes lung tumorigenesis by triggering IKKβ- and JNK1-dependent inflammation. Cancer Cell 2010;17:89–97.
41. Cornfield J, Haenszel W, Hammond EC, Lilienfeld AM, Shimkin MB, Wynder EL. Smoking and lung cancer: recent evidence and a discussion of some questions. Int J Epidemiol 2009;38:1175–91.