Research Article

Cancer Epidemiology, Biomarkers & Prevention

Reproductive, Lifestyle, and Anthropometric Risk Factors for Cancer in Elderly Women

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Abstract

Background: With an increasing elderly population, the United States will experience an increased cancer burden in the coming years. We evaluated associations between anthropometric, lifestyle, and reproductive factors and risk of breast, ovarian, and colorectal cancer in a prospective study of postmenopausal women with a focus on diagnoses occurring among very elderly women (≥75 years).

Methods: For each cancer type, we estimated associations with relevant exposures in 2 age bands (<75 vs. ≥75 years of age). During 22 years of follow-up, 322 ovarian, 1,311 colon, 315 rectal, and 2,664 breast cancers occurred among 37,459 postmenopausal women (mean age at baseline 62 years, range 55–71 years).

Results: For ovarian cancer, we identified few significant associations in either age band. Colon cancer cases had a higher body mass index and were less likely to report estrogen or aspirin use than non-cases, yet these associations were consistent in both age bands. Few risk factors were identified for rectal cancer in women of 75 years of age or more. For breast cancer, notably different patterns were revealed, with alcohol consumption associated with risk in the younger group and previous hysterectomy associated with risk only in the older group.

Conclusion: These analyses suggest some important differences in risk factors for cancer depending on the age at diagnosis.

Impact: This study suggests that etiologic differences may exist in cancers occurring in the very elderly women. The ongoing demographic shift in the United States provides a strong rationale for studies evaluating cancer etiology in the elderly. *Cancer Epidemiol Biomarkers Prev; 22(4); 681–7. ©2013 AACR.*

Introduction

The population of the United States is currently undergoing major demographic changes, including a striking projected increase in elderly individuals in the next several decades (1). Because the incidence of most cancers, including ovarian, breast, and colorectal, increases dramatically starting in middle age, rapid growth in the elderly population will lead to dramatic increases in the number of cancers diagnosed (2), providing a strong rationale for cancer studies in the elderly. To date, most studies on cancer in aging populations have focused on treatment, outcomes, and functional consequences of cancer; few studies have evaluated risk factors that could differ from younger individuals and inform etiology and prevention.

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Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

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doi: 10.1158/1055-9965.EPI-12-0966

Anthropometric (e.g., body mass index; BMI) and lifestyle factors (e.g., alcohol consumption) are well-established risk factors for breast and colorectal cancers (3–7). Reproductive factors (e.g., parity) are well-established risk factors for ovarian (8) and breast (9) cancers. Exogenous hormone use, including hormone replacement therapy and oral contraceptive use, are also associated with breast (10, 11), ovarian (8), and colorectal (12, 13) cancers. Studies have identified risk heterogeneity by tumor characteristics (14, 15). Some studies have reported risk differences by age, but few have specifically evaluated cancer that occurs during elderly ages (>75 years). Because tumor characteristics differ in elderly women (16, 17), it is likely that there may also be differences by age at diagnosis. Given the importance of anthropometric, lifestyle, and reproductive factors in the etiology of cancer, we have focused our analysis on these risk factors.

In a previous analysis including cases diagnosed from 1986 to 2001, we evaluated risk factors for breast cancer in elderly women (18). Here, we report an updated analysis with an additional 7 years of follow-up. We also compare risk factors for ovarian, colon, and rectal cancers in women diagnosed before and after the age of 75 years. We hypothesized that the risk factors associated with cancers that develop in the elderly are different from those that occur earlier in postmenopausal women.

Materials and Methods

Detailed descriptions of the Iowa Women's Health Study (IWHS) have been published (19–21). Briefly, a random sample of women ages 55 to 69 years listed on the State of Iowa's driver's license list was contacted by mail to complete a survey in January 1986; a total of 41,836 women responded (42%). The baseline survey assessed reproductive history, anthropometric data, and risk factors for cancer such as smoking and physical activity. Incident cancer cases were identified through computer matching from 1986 through 2008 using the Health Registry of Iowa, part of the National Cancer Institute's Surveillance Epidemiology and End Results Program. The annual migration rate from Iowa among the IWHS participants was less than 1%, meaning a nearly complete follow-up of incident cancers.

Women were excluded if they were premenopausal ($n = 547$) or reported a history of cancer (other than nonmelanoma skin cancer; $n = 3{,}830$) at the time of the baseline questionnaire (1986). For the ovarian cancer analysis, women were also excluded if they had a bilateral oophorectomy at baseline ($n = 6{,}598$) or if their cancer had a nonepithelial histology ($n = 20$). For the colorectal cancer analyses, additional exclusion criteria included histology of their cancer other than adenocarcinoma ($n = 19$ colon, 8 rectal) or carcinoma *in situ* ($n = 48$ colon, 20 rectal). For the breast cancer analyses, we excluded women who had a history of mastectomy at baseline ($n = 354$), nonepithelial histology ($n = 9$), or carcinoma *in situ* ($n = 413$).

At baseline, women were asked about their menstrual and reproductive history. Estrogen use was determined by asking participants whether they had ever used estrogen or any estrogen-containing pills other than oral contraceptive pills. A measuring tape was sent for a friend to measure the woman's waist and hip circumference to calculate waist-to-hip ratio (WHR; ref. 22). BMI was calculated from self-reported current weight and height (kg/m^2). Information on smoking status, alcohol consumption, and leisure physical activity was also collected. For this analysis, categorical variables were created on the basis of the distribution of the data in the IWHS or following standard definitions (e.g., BMI) for age at baseline (<60, 60–64, ≥65), BMI (<25 kg/m^2, 25–29 kg/m^2, ≥30 kg/m^2), WHR (quartiles), age at menarche (≤12, >12 years), age at menopause (≤50, >50 years), number of live births (0, 1–2, 3–4, 5 or more), and history of hysterectomy, estrogen use, and oral contraceptive use (yes, no). We also evaluated a 3-level physical activity index (low, moderate, and high), smoking status at baseline (never, former, and current), and alcohol consumption at baseline (yes, no).

Statistical analysis

For each cancer type, 2 age bands were formed. In the first age band, all study participants were followed until they reached the age of 75 years unless they were censored because they (i) were diagnosed with the cancer of interest, (ii) died, or (iii) were lost to follow-up. Women who were not censored for 1 of these 3 reasons before the age of 75 years entered the analysis of the follow-up starting at the age of 75 years. We computed person-time (years) from the study baseline until the age of 75 years for the first age band and from the time that each study participant reached the age of 75 years until the end of follow-up for the second age band. We computed age-adjusted and multivariate-adjusted HR and their 95% confidence intervals (CI) using Cox proportional hazards regression (SAS Institute). Reported P values are 2-sided. Tests for interaction were also conducted considering intraindividual correlations between the 2 age bands.

Results

After exclusion of premenopausal women and women with a personal history of cancer at baseline, there were 37,459 women available for analysis (mean age at baseline 62 years, range 55–71 years). During the 22-year follow-up period, we identified 322 incident ovarian cancers, 1,311 incident colon cancers, 315 incident rectal cancers, and 2,664 incident breast cancers. Of these, 135 ovarian, 707 colon, 132 rectal, and 1,071 breast cancers occurred in women aged 75 years or more. As expected, incidence of all 4 cancers was higher in the 75-year-old or more age band (Table 1).

Ovarian cancer

For the ovarian cancer analysis, the younger age band included 30,841 women (341,361 person-years of follow-up), whereas the older age band included 24,373 women (214,921 person-years of follow-up). The median age at diagnosis was 73 years (range 57–90 years). Older age at baseline was the only significantly associated risk factor

Table 1. Incidence rates for ovarian, colon, rectal, and breast cancer by age group, IWHS, 1986 to 2008

	<75 years			≥75 years		
Cancer	Cases (*N*)	Person-years at risk	Incidence rate (per 100,000)	Cases (*N*)	Person-years at risk	Incidence rate (per 100,000)
Ovarian	187	341,359	54.8	135	214,921	62.8
Colon	604	423,687	142.6	707	271,264	260.6
Rectal	183	350,469	52.2	132	158,727	83.2
Breast	1,593	339,686	469.0	1,071	146,834	729.4

for ovarian cancer in women aged 75 years old or more (Table 2). Among women less than 75 years old, a high level of physical activity at baseline and a positive family history of ovarian cancer increased risk, whereas increased number of live births was associated with reduced risk (Table 2). While the magnitude of association differed by age band, these differences did not achieve statistical significance ($P_{interaction} > 0.05$). There was little difference between cases and non-cases in either age band for smoking, age at menarche or menopause, history of hysterectomy, or hormone use (Supplementary Table S1).

Colon cancer

The younger age band for the colon and rectal cancer analyses included 37,432 women and 423,387 person-years of follow-up. The older age band included 30,814 women with 271,264 person-years of follow-up. The median age at colon cancer diagnosis was 75 years (range 56–92 years). Higher BMI and a reported diagnosis of diabetes were associated with an increased risk of colon cancer, whereas reported estrogen or aspirin use were associated with reduced risk in both age bands (Table 2). Smoking was significantly associated with colon cancer in the younger age band, although the *P* value for interaction did not reach statistical significance. We observed a significant interaction with age at baseline ($P_{interaction} = 0.0002$), with an increased risk observed only in the younger age band. None of the other variables was associated with colon cancer in either age band (Supplementary Table S2).

Rectal cancer

For rectal cancer, the median age at diagnosis was 73 years (range 55–89 years). Oral contraceptive use was associated with a reduced risk for rectal cancer among women 75 years of age or more (HR = 0.46; 95% CI, 0.23–0.91). No other significant associations were observed in this age band (Table 2 and Supplementary Table S3). In the younger age band, older age at baseline and current smoking increased the risk for rectal cancer, whereas estrogen use was associated with a reduced risk (Table 2). In the analysis stratified by age band, we observed a significant interaction *P* value for oral contraceptive use ($P_{interaction} = 0.04$), although this finding should be interpreted with caution given the small number of oral contraceptive users. The interaction *P* values for age at baseline, smoking, and estrogen use were not statistically significant ($P \geq 0.05$).

Breast cancer

The younger age band included 37,096 women (412,633 person-years), and the older age band included 29,473 women (256,889 person-years) with a median age of 72 years (range 55–92 years) at breast cancer diagnosis. Higher reported BMI, older age at menopause, and later age at first birth were associated with increased risk of breast cancer in the older group, whereas a higher number of live births was associated with a reduced risk (Table 2). In addition to these associations, WHR, current smoking at baseline, age at menarche, alcohol consumption at baseline, and aspirin or nonsteroidal anti-inflammatory drug (NSAID) use were significantly associated with breast cancer risk in the younger age band (Table 2). Some notably different patterns were revealed when we compared the 2 age bands. We observed significant interactions between age band and age at baseline ($P_{interaction} = 0.006$), alcohol consumption at baseline ($P_{interaction} = 0.02$), and history of hysterectomy ($P_{interaction} = 0.03$), with alcohol associated with risk in the younger age band and hysterectomy associated with risk only in the older age band (Table 2).

Discussion

Few studies have focused on the risk factors for cancer in elderly women; therefore, etiologic differences in this growing subgroup are currently not well understood. We evaluated associations between established anthropometric, lifestyle, and reproductive factors, and 4 common cancers in a large cohort of postmenopausal women with the goal of identifying differences in very elderly women. Consistent with the literature (8), few risk factors were observed for ovarian cancer in either age group. For colon and rectal cancers, the associations were very consistent when the analysis was stratified by age. We did observe several notable differences in breast cancer risk factors by age, specifically for alcohol consumption at baseline and history of hysterectomy. The interaction *P*values were also borderline significant for the differences by age at menarche and smoking status at baseline.

While anthropometric variables, including high BMI and WHR, are well-established risk factors for breast and colorectal cancers in mid-life (3, 4, 23), the association is not well established in the elderly. Associations between indicators of body size and chronic conditions such as cardiovascular disease in older people are not as strong or as consistent as they are in younger individuals. Indeed, high BMI has been found to be associated with increased survival in elderly Americans (24). This inconsistency may be due to survival bias, competing mortalities, smoking, and unintentional weight loss (25). Here, the increased risk of breast and colon cancer associated with high BMI observed in the younger age band persisted in women 75 years of age or more.

Lifestyle factors, such as physical activity (5), smoking (6), and alcohol consumption (7), also have known associations with breast and colorectal cancers. Data from the Behavioral Risk Factor Surveillance System survey (26) show that the prevalence of smoking and alcohol consumption declines in women more than the age of 65 years, therefore, their impact as risk factors may be reduced in the elderly women. We observed a significant association between baseline smoking and both colon and rectal cancers in the younger age band. In the older age band, the association was borderline significant for colon cancer, whereas there was no association for rectal cancer.

Table 2. Potential risk factors for ovarian, colon, rectal, and breast cancers by age band at diagnosis[a]

	< 75 years old				≥75 years old				
	Cases	Person-years	HR (95% CI)[b]	*P* or P_{trend}	Cases	Person-years	HR (95% CI)[b]	*P* or P_{trend}	$P_{interaction}$[c]
Ovarian cancer									
Age at baseline									
<60	92	159,819	1.0	21	43,137	1.0			
60–64	58	119,523	0.87 (0.61–1.25)	46	78,298	1.31 (0.75–2.27)			
≥65	37	62,017	1.20 (0.77–1.87)	0.64	68	93,486	1.68 (0.98–2.88)	0.047	0.30
Physical activity level									
Low	71	159,835	1.0	57	42,905	1.0			
Moderate	53	91,546	1.27 (0.88–1.83)	44	88,953	1.23 (0.82–1.85)			
High	58	83,840	1.55 (1.08–2.22)	0.02	30	83,063	0.97 (0.62–1.53)	0.97	0.12
Family history of ovarian cancer[d]									
No	173	332,244	1.0	132	209,471	1.0			
Yes	14	9,118	3.16 (1.83–5.45)	<0.0001	3	5,450	0.93 (0.30–2.93)	0.90	0.06
Number of live births									
0	23	27,255	1.0	13	19,697	1.0			
1–2	59	101,834	0.69 (0.42–1.13)	41	70,019	0.91 (0.48–1.74)			
3–4	74	138,568	0.60 (0.37–0.96)	59	83,250	1.13 (0.60–2.11)			
5+	31	71,782	0.45 (0.25–0.79)	0.005	21	40,477	0.85 (0.41–1.74)	0.98	0.09
Colon cancer									
Age at baseline									
<60	236	201,656	1.0	109	56,755	1.0			
60–64	228	147,680	1.57 (1.29–1.92)	281	99,470	1.29 (1.02–1.64)			
≥65	140	74,351	2.28 (1.78–2.92)	<0.0001	317	115,039	0.26 (0.99–1.60)	0.14	0.0002
Body mass index									
<25	198	167,647	1.0	244	106,267	1.0			
25–<30	235	156,583	1.28 (1.06–1.56)	274	103,759	1.18 (0.99–1.41)			
≥30	171	99,157	1.44 (1.16–1.78)	0.0006	189	61,237	1.38 (1.13–1.69)	0.001	0.69
Smoking									
Never	370	274,486	1.0	495	191,764	1.0			
Past	130	80,119	1.27 (1.04–1.56)	115	47,178	0.97 (0.79–119)			
Current	96	62,381	1.27 (1.01–1.60)	0.01	79	27,915	1.22 (0.96–1.56)	0.22	0.53
Estrogen use									
Never	419	262,588	1.0	454	166,168	1.0			
Ever	185	160,799	0.71 (0.60–0.85)	0.0002	253	105,196	0.88 (0.75–1.03)	0.11	0.10
History of diabetes									
No	553	399,956	1.0	655	258,939	1.0			
Yes	51	22,877	1.35 (0.99–1.84)	0.06	51	11,928	1.59 (1.18–2.14)	0.002	0.54
Aspirin or NSAID use[e]									
No	100	60,565	1.0	125	40,488	1.0			
Yes	320	288,148	0.70 (0.56–0.89)	0.003	460	188,029	0.78 (0.64–0.95)	0.02	0.45
Rectal cancer									
Age at baseline									
<60	73	202,603	1.0	23	57,570	1.0			
60–64	65	147,866	1.40 (0.97–2.01)	48	101,157	1.11 (0.66–1.89)			
≥65	45	74,575	2.34 (1.51–3.63)	0.0002	61	117,037	1.18 (0.69–2.00)	0.56	0.05
Smoking									
Never	105	275,540	1.0	90	194,832	1.0			
Past	38	80,560	1.23 (0.84–1.80)	26	48,062	1.23 (0.80–1.91)			
Current	35	62,541	1.68 (1.13–2.49)	0.01	14	28,401	1.19 (0.67–2.11)	0.36	0.54
Estrogen use									
Never	129	263,669	1.0	87	169,110	1.0			
Ever	54	161,375	0.70 (0.50–0.96)	0.03	45	106,654	1.00 (0.67–1.48)	1.00	0.37
Oral contraceptive use									
No	140	332,079	1.0	122	234,829	1.0			
Yes	43	92,964	1.27 (0.88–1.83)	0.20	10	40,935	0.46 (0.23–0.91)	0.03	0.04

(Continued on the following page)

Table 2. Potential risk factors for ovarian, colon, rectal, and breast cancers by age band at diagnosis[a] (Cont'd)

	< 75 years old				≥75 years old				
	Cases	Person-years	HR (95% CI)[b]	*P* or P_{trend}	Cases	Person-years	HR (95% CI)[b]	*P* or P_{trend}	$P_{interaction}$[c]
Breast cancer									
Age at baseline									
<60	687	196,272	1.0	207	53,319	1.0			
60–64	613	143,414	1.35 (1.19–1.52)	414	93,515	1.10 (0.92–1.32)			
≥65	293	72,946	1.35 (1.15–1.58)	<0.0001	450	110,055	1.07 (0.89–1.29)	0.59	0.006
BMI									
<25	547	163,218	1.0	353	100,980	1.0			
25–< 30	606	152,625	1.18 (1.04–1.33)	449	98,029	1.30 (1.12–1.52)	0.0006		
≥30	440	96,579	1.35 (1.17–1.55)	<0.0001	269	57,880	1.35 (1.13–1.62)	0.001	0.80
WHR									
Q1 (0.335–0.777)	383	110,216	1.0	246	63,163	1.0			
Q2 (>0.777–0.832)	367	104,033	0.97 (0.83–1.12)	258	65,248	0.99 (0.82–1.18)			
Q3 (>0.832–0.892)	388	100,772	1.01 (0.87–1.18)	271	65,577	0.99 (0.82–1.19)			
Q4 (>0.892–2.836)	448	95,813	1.18 (1.01–1.38)	0.02	290	61,990	1.05 (0.87–1.28)	0.63	0.26
Family history of breast cancer[d]									
No	1,138	318,733	1.0	732	198,514	1.0			
Yes	455	93,899	1.35 (1.21–1.51)	<0.0001	339	58,374	1.57 (1.37–1.79)	<0.0001	0.09
Age at menarche									
≤12	725	175,292	1.0	432	105,074	1.0			
>12	855	232,907	0.90 (0.81–1.00)	0.048	631	148,502	1.06 (0.94–1.21)	0.34	0.05
Age at menopause									
< 50	778	215,226	1.0	463	130,677	1.0			
≥ 50	815	197,407	1.15 (1.04–1.27)	0.008	608	126,211	1.35 (1.19–1.53)	<0.0001	0.04
Number of live births									
0	160	36,201	1.0	107	25,838	1.0			
1–2	511	125,740	0.57 (0.39–0.84)	384	84,903	0.70 (0.44–1.11)			
3–4	660	166,743	0.58 (0.41–0.82)	409	98,813	0.64 (0.42–0.98)			
5+	262	83,948	0.45 (0.32–0.65)	<0.0001	171	47,335	0.57 (0.37–0.88)	0.001	0.50
Age at first live birth									
<20	285	86,040	1.0	159	44,593	1.0			
20–24	723	193,329	1.12 (0.98–1.29)	463	112,881	1.18 (0.98–1.42)			
25–29	308	74,508	1.17 (0.99–1.39)	247	55,451	1.18 (0.95–1.46)			
≥30	108	20,329	1.45 (1.14–1.83)	0.003	89	16,613	1.40 (1.06–1.85)	0.03	0.43
Nulliparous	160	36,201	1.06 (0.84–1.34)	107	25,838	1.05 (0.78–1.42)			
Smoking									
Never	998	267,781	1.0	744	181,870	1.0			
Past	313	78,153	1.06 (0.93–1.21)	209	44,314	1.17 (1.00–1.38)			
Current	265	60,483	1.25 (1.08–1.44)	0.004	100	26,458	0.99 (0.80–1.24)	0.43	0.22
Alcohol consumption									
No	832	228,828	1.0	631	149,329	1.0			
Yes	761	183,805	1.20 (1.08–1.33)	0.0007	440	107,559	0.98 (0.86–1.11)	0.73	0.02
History of hysterectomy									
No	1,088	276,458	1.0	703	174,329	1.0			
Yes	505	136,174	1.02 (0.91–1.16)	0.71	368	82,530	1.31 (1.13–1.51)	0.0003	0.03
Aspirin or NSAID use[e]									
No	256	56,990	1.0	159	36,932	1.0			
Yes	1,040	280,606	0.82 (0.71–0.94)	0.005	737	177,556	0.94 (0.78–1.12)	0.46	0.28

[a]Includes only risk factors where the association was significant in at least one of the risk sets. All remaining risk factors are included in the Supplementary Tables.

[b]Adjusted for age at baseline, BMI (kg/m^2), physical activity level (low, moderate, high), smoking (never, past, current), age at menarche (ovarian, breast), estrogen use (colon, rectal), WHR (breast), age at menopause (breast), number of live births (breast), age at first live births (breast), and alcohol intake (breast).

[c]*P* values for tests whether HRs differ by the follow-up (<75 y vs. ≥75 y)

[d]Family history among first- and second-degree relatives.

[e]Analysis was restricted to women who were alive and responded to the follow-up 3 (1992) questionnaire.

For breast cancer, we observed a significant association for smoking and alcohol consumption at baseline in the younger group but no association in the older age group, with evidence for a significant interaction for alcohol consumption. The well-established increased risk of mortality in both middle-aged (27) and elderly (28) smokers supports mortality due to other causes as an explanation for these results. Misclassification of exposure may also explain differences between age bands because smoking and alcohol consumption were measured at baseline, and exposure status could have changed or become less relevant during the follow-up period.

Reproductive factors are well-established risk factors for breast cancer (9). Older age at menarche, younger age at menopause, young age at first pregnancy, and increased number of pregnancies have been consistently associated with a reduced risk of breast cancer. Consistent with a previous case–control study (29) and a previous analysis in the IWHS (18), the association with age at menarche was observed only in the younger age band, whereas the association with age at menopause remained important in the older band. In this previous analysis of breast cancer risk factors by age in the IWHS (18), a high number of births, BMI, and family history of breast cancer were found to be associated with risk of breast cancer in all age groups, whereas nulliparity and age at first live birth were not associated with risk in women diagnosed after age 75 years. In this analysis with an additional 7 years of follow-up, the magnitude of the association for the increased risk associated with age at first live birth was similar in the 2 age bands. The previous analysis did not evaluate associations with lifestyle factors or history of hysterectomy; therefore, we cannot compare our findings for these risk factors.

Full-term pregnancy and oral contraceptive use both seem to reduce the risk of ovarian cancer (8). Less conclusive evidence suggests that early age at menarche, late age at menopause, and obesity increase the risk of ovarian cancer (8). Number of live births was the only reproductive factor associated with ovarian cancer in our study and this association seemed to be stronger in the younger age band, although the interaction *P* value did not reach statistical significance. The small number of women who reported using oral contraceptives limited our power to evaluate this association.

Hormones have been posed as an explanation for the lower colorectal cancer risk in women compared with men for many years (30); however, the studies reporting associations between reproductive factors and colorectal cancer have been inconsistent (31). Exogenous hormones, including hormone replacement therapy (12) and oral contraceptive use (13), have been more consistently associated with reduced colorectal cancer risk. Postmenopausal estrogen use was associated with reduced risk of colon cancer in both age bands, whereas there was no association with oral contraceptive use. For rectal cancer, we observed a significant association for postmenopausal estrogen use in the younger age band and a significant association for oral contraceptive use in the older age band; however, the interaction *P* value for estrogen use failed to reach statistical significance. The explanation for the difference observed for oral contraceptive use is unclear, although chance could play a role given the large number of comparisons we have made.

The prospective nature of the study, long duration of follow-up, and the large number of women in the older age band (>75 years) are important strengths. Most cohort members contributed person-time in the 2 age bands considered for analysis. We recognize that the choice of age 75 years as a cutoff for the older age band is somewhat arbitrary; however, our primary objective was to evaluate risk factors for common cancers in the very elderly. In addition to adjusting for age to control for any possible birth cohort effects, we also adjusted for several potential confounders. Limitations include generalizability, given that participants were nearly all non-Hispanic White women living in one state, possessed a driver's license, and were able to complete a detailed questionnaire. Furthermore, some reported events (e.g., smoking and alcohol consumption) could change over time, and therefore misclassification could increase. However, most reproductive factors explored would unlikely change after baseline among postmenopausal women. In addition, we were unable to evaluate differences in risk factors for breast cancer by hormone receptor status. Finally, given the limited number of ovarian and rectal cancers included, power is limited to detect interactions with age. Nevertheless, as we previously reported for breast cancer in the elderly (18), these analyses suggest some important differences in risk factors for cancer depending on age at diagnosis. It will be of interest to see whether these results are confirmed in other large cohort studies.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: J.N. Poynter, J.A. Ross
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Grant Support

This work was supported in part by National Cancer Institute R01 CA39742.

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Received August 17, 2012; revised January 24, 2013; accepted February 2, 2013; published OnlineFirst February 19, 2013.

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