

Husband's smoking status and breast cancer risk in Japan: From the Takayama study

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The effects of smoking on breast cancer remain unclear. We assessed the associations of subjects' or husbands' smoking status with breast cancer incidence in a population-based prospective study in Japan. The subjects were 15 719 women aged 35 years or older. The follow up was conducted from September 1992 to March 2008. Cancer incidence was mainly confirmed through regional population-based cancer registries. Breast cancer was defined as code C50 according to the International Classification of Diseases and Health Related Problems, 10th Revision. Lifestyle, including smoking status, was assessed with a self-administered questionnaire. Alcohol consumption was assessed with a validated food-frequency questionnaire. After multivariate adjustments for age, body mass index, alcohol consumption, physical activity, education, age at menarche, age at first delivery, menopausal status, number of children and history of hormone replacement therapy, active smoking was not associated with the risk of breast cancer. Compared with never smokers whose husband had never smoked, the risks of breast cancer were 1.98 (95% CI: 1.03–3.84) among never smokers whose husband was a current smoker of 21 cigarettes per day or more. The increased risk of breast cancer among women having a smoking husband was pronounced among those who did not habitually consume alcohol. These results suggest that exposure to smoke from husbands is a potential risk factor for breast cancer. The impact of alcohol consumption on the increased breast cancer risk from passive smoking needs to be addressed in further studies.

Breast cancer is the most common cancer in women worldwide. In recent years in Japan, breast cancer has shown a continuously increasing trend for both incidence and mortality, and is the top cause of cancer incidence in women,⁽¹⁾ although breast cancer incidence in Japan still remains lower than in Europe and the USA.⁽²⁾

In spite of the biological plausibility of a positive association between cigarette smoking and breast cancer risk, epidemiological studies have shown inconsistent results. Several meta-analyses on the association of active^(3–7) and passive^(4,8–11) smoking with breast cancer risk have been published, and include different subsets of studies. In 2002, a meta-analysis of 53 epidemiological studies showed no overall association between active smoking and breast cancer risk after taking into account the effects of alcohol⁽³⁾ because alcohol consumption is a risk factor for breast cancer.^(12,13) However, Gaudet *et al.*⁽⁷⁾ conduct a meta-analysis of 15 recent cohort studies and demonstrate a positive association between active smoking and breast cancer risk, independent of the effect of alcohol. They also show that the associations are found among former and current drinkers, but not among never drinkers from their US cohort (*P*interaction = 0.11). For passive smoking, an increased risk of breast cancer among women who were

exposed to smoke has been reported, particularly from case-control studies, whereas the evidence from cohort studies was inconclusive.^(4,8–10,14) The most recent meta-analysis including 10 cohort studies by Yang *et al.*⁽¹¹⁾ reported the lack of an association between passive smoking and breast cancer among non-smokers. Thus, additional assessment of smoking and breast cancer is needed.

In this study, we assessed the associations between subjects' or husband's smoking status and breast cancer incidence in a population-based prospective cohort study in Japan. We further examined whether or not the associations were modified by menopausal status and alcohol consumption.

Materials and Methods

Participants and design. The study participants were 36 990 unhospitalized residents of Takayama City, Gifu, Japan, aged 35 years or older in September 1992. They were enrolled in the Takayama study, a prospective cohort study. The details of the population-based cohorts have been described previously elsewhere.⁽¹⁵⁾ A total of 31 552 residents (85.3%) completed a baseline self-administered questionnaire which included questions on demography, anthropometric characteristics, medical

history, smoking status, physical activity and diet. Female participants were also asked about their reproductive characteristics, including age at menarche, age at first delivery, menopausal status, parity number and history of hormone replacement therapy.

In the baseline questionnaire, the subjects were asked about their smoking habits; never, former or current smokers. Smokers were defined as people who had smoked a total of at least 20 packs of cigarettes in their life. Former and current smokers were asked to choose from among five options for the number of cigarettes smoked per day; 5 cigarettes or less, 6 to 10 cigarettes, 11 to 20 cigarettes, 21 to 30 cigarettes, or 31 cigarettes or more. Although the questionnaire did not include the smoking status of each subject's spouse, we identified married couples by the following conditions: (i) the pair consisted of a man and a woman with the same household number; (ii) the difference between their ages was <15 years; (iii) both the man and the woman indicated their marital status as "married"; and (iv) that he or she belonged to only one pair. The details have been described elsewhere.⁽¹⁶⁾ The response about smoking status elicited from the spouse's questionnaire was used as the index of husband's smoking.

Dietary data, including alcohol consumption, were assessed using a 169-item semi-quantitative food frequency questionnaire (FFQ). In the questionnaire, participants were asked how often on average they consumed each of the food items listed, and what the usual serving size of each item was during the past year. The questions on alcohol intake covered six different types of liquor: sake, shochu, beer, light beer, wine and hard liquor. For each item, the questions included nine categories of frequency (never/less than once per month, once per month, 2–3 times per month, once per week, 2–3 times per week, 4–6 times per week, once per day, 2–3 times per day and 4 times per day or more) and four categories of each serving size (the number of cups, glasses or bottles). Individual nutrient intake was also estimated from the frequency of ingestion and portion size using the Japanese Standard Table of Food Composition (5th revised and enlarged edition), published by the Science and Technology Agency of Japan.⁽¹⁷⁾ The validity and reproducibility of the questionnaire were previously reported to be reliable.⁽¹⁸⁾ The Spearman correlation coefficient between the FFQ and 12-day diet records kept over a 1-year period for alcohol intake was 0.64 for women.

Physical activity was assessed by asking participants how much time on average they spent during the past year on activities from a list of strenuous sports, vigorous work and moderate activities. The number of hours per week spent in each activity was multiplied by the corresponding energy expenditure, expressed as a metabolic equivalent (MET), and the sum of the product was counted as the physical activity score (MET·h/week). The details, including its validity, are described elsewhere.⁽¹⁹⁾

Among 17 125 women included in the baseline survey (1 September 1992), 543 who were diagnosed with breast cancer before the baseline and/or reported a positive history of any cancers at the baseline were excluded. The residual women were followed until the end of March 2008. Migration data were obtained from the residential registers. During the study period, 929 persons (5.6%) moved out of the study area, and the date of emigration was unknown for 141 women (0.9%). The incidence of cancer was mainly confirmed through two regional population-based cancer registries in Gifu. Information was also collected from a local base hospital, which had played a leading role in medical care for the residents in the

study area. The causes of cancer were coded according to the International Classification of Diseases and Health Related Problems, 10th Revision. Breast cancer was defined as code C50. The mortality-to-incidence ratio for breast cancer was 0.16, and 6.0% of patients were ascertained by death certificate-only registration, indicating the very complete cancer registration of this cohort. This study was approved by the ethical board of the Gifu University Graduate School of Medicine.

Statistical analyses. After female subjects with neither information on smoking status of their own nor of their husband were excluded, our analysis finally included 15 719 women. For smoking status of the husbands, current smokers were re-categorized into one of two groups: smokers of 20 cigarettes or less per day, or smokers of 21 cigarettes or more per day.

The end of follow up was determined as the date of breast cancer diagnosis, the date of emigration from the study area, the date of death or the end of the study, whichever came first. For women who moved away on a date unknown, their last confirmed date of residence in the study area was used as their censored date. Relative risks and 95% confidence intervals (CI) for breast cancer were estimated for the groups of smoking status using the Cox proportional hazards regression model. The reference group was set as the never smokers. To eliminate the impact of active smoking, the analyses for husband's smoking status and breast cancer risk were conducted among never female smokers. To test a linear trend for breast cancer risk by smoking status of the husbands, we assigned 0 for never and former smokers, 10 for smokers of 20 cigarettes or less per day, and 21 for smokers of 21 cigarettes or more per day, and inputted them as continuous variable into the models.

Covariates included in the models were the following potential confounders: age (years, continuous), body mass index (quartiles), physical activity score (continuous), alcohol consumption (g/day), years of education (≤ 8 , 9–11, 12–14, ≥ 15 years), age at menarche (≤ 12 , 13–14, 15–16, ≥ 17 years), age at first delivery (non-parous, ≤ 20 , 20–25, 26–30, ≥ 31 years), menopausal status (premenopausal, postmenopausal ≤ 49 years, postmenopausal ≥ 50 years), parity number (0, 1, 2, ≥ 3) and history of hormone replacement therapy (yes, no). Indicator terms were specifically created for missing data of categorical covariates.

These analyses were repeated among never smokers after being stratified to premenopausal and postmenopausal women at the baseline, because menopausal status was known to affect the etiology of breast cancer. To clarify whether alcohol drinking modifies the effects of smoking on breast cancer, we further examined the associations stratified by alcohol consumption (non-drinkers or drinkers). Tests for interaction were performed using the likelihood ratio test.

All analyses were conducted using the SAS computer program, version 9.3 (SAS Institute). *P*-values were calculated by a two-sided test. A *P*-value < 0.05 was considered statistically significant in all analyses.

Results

Among 15 719 subjects, 14 830 (94.3%) responded to the questions about their own smoking status. It was ascertained that 10 599 participants had husbands, and 10 427 (98.4%) husbands responded to the questions about smoking status.

The characteristics of participants were shown as the mean (standard deviation) or number (percentage) of each category, according to the subjects' own smoking status and each of

Table 1. Characteristics of study subjects at baseline in Takayama study

	Subject's smoking status			Husband's smoking status			
	Never	Former	Current	Never	Former	Current (0 < to 20 cigarettes/day)	Current (≥21 cigarettes/day)
<i>N</i>	12 219	685	1926	1709	3192	3280	2246
Age (y)†	55.6 (13.0)	58.2 (15.5)	52.0 (12.2)	52.7 (11.0)	55.8 (11.1)	52.7 (10.5)	47.8 (8.7)
Height (cm)†	151.9 (6.3)	152.3 (6.4)	153.7 (6.0)	152.6 (6.1)	152.1 (6.0)	152.6 (5.7)	154.1 (5.5)
Weight (kg)†	50.9 (7.6)	51.0 (8.5)	51.2 (8.0)	51.8 (7.2)	51.1 (7.3)	51.6 (7.3)	52.4 (7.4)
Body mass index (kg/m ²)†	22.0 (2.9)	22.0 (3.0)	21.7 (3.0)	22.3 (2.9)	22.1 (2.8)	22.1 (2.8)	22.1 (2.9)
Age at menarche‡							
≤12 years	1587 (13.3)	84 (12.7)	262 (13.9)	255 (15.3)	356 (11.4)	451 (14.1)	426 (19.2)
13–16 years	8670 (72.6)	467 (77.4)	1389 (73.8)	1210 (72.4)	2320 (74.1)	3448 (73.2)	1618 (73.0)
≥17 years	1680 (14.1)	112 (16.9)	232 (12.3)	206 (12.3)	453 (14.5)	410 (12.8)	174 (7.8)
Menopausal status‡ (premenopausal)	4942 (41.2)	240 (35.8)	1008 (53.3)	807 (48.1)	1116 (35.6)	1484 (46.0)	1466 (65.8)
Birth experience (none)‡	965 (8.1)	103 (15.8)	244 (13.1)	77 (4.6)	129 (4.2)	142 (4.4)	99 (4.5)
History of hormone replacement therapy (yes)‡	799 (6.8)	50 (7.9)	172 (9.5)	120 (7.4)	249 (8.2)	222 (7.2)	169 (7.8)
Total energy intake (kcal/day)†	2128 (778)	2062 (738)	2220 (870)	2177 (742)	2122 (746)	2167 (742)	2219 (785)
Alcohol consumption (g/day)†	6.3 (13.4)	9.5 (18.1)	17.8 (29.8)	6.6 (13.6)	6.7 (14.0)	6.9 (13.9)	9.6 (20.3)
Physical activity score† (MET·h/week)	19.3 (29.8)	16.7 (30.0)	18.8 (29.3)	22.1 (31.1)	19.2 (30.5)	20.5 (30.6)	23.6 (34.5)
Smoking status of husband‡							
Never	1505 (18.5)	29 (8.7)	73 (7.0)				
Former	2570 (31.5)	129 (38.7)	170 (16.2)				
Current (0 < to 20 cigarettes/day)	2478 (30.4)	96 (28.8)	376 (35.8)				
Current (≥21 cigarettes/day)	1602 (19.6)	79 (23.7)	431 (41.1)				

†Mean (standard deviation). ‡Number (percentage).

their husbands, as shown in Table 1. Former smokers were generally the oldest and current smokers were generally the youngest. Women who had ever smoked were likely to drink more, to have fewer experiences of childbirth, and to have histories of hormone replacement therapy. The subjects' own smoking status was related to the smoking status of their husbands.

Table 2 shows the associations of smoking habits of subjects and their husbands with incidence of breast cancer. Active smoking by the subjects was not associated with the risk of breast cancer in the multivariate-adjusted model. When sub-

jects were limited to never smokers, compared with women whose husbands had never smoked, the hazard ratio was 1.98 (95% CI: 1.03–3.84) among women whose husband was a current smoker of 21 cigarettes per day or more. The hazard ratios of breast cancer grew gradually higher along with the numbers of cigarettes husbands currently smoked per day (*P* for linear trend = 0.023).

When the analyses were repeated among never smokers by menopausal status at the baseline, increased risks of breast cancer among women with a husband who smoked were observed among premenopausal and postmenopausal women

Table 2. Associations of smoking habits of subject and her husband with incidence of breast cancer from Takayama study

	Number of subjects	Incidence	Person years	Age-adjusted HR	(95% CI)	Multivariate-adjusted HR†	(95% CI)
Subject's smoking status	14 830	166					
Never	12 219	142	171 449	1.00	(reference)	1.00	(reference)
Former	685	5	8772	0.71	(0.29, 1.73)	0.67	(0.28, 1.65)
Current	1926	19	26 415	0.83	(0.51, 1.34)	0.90	(0.55, 1.47)
(Among never smokers)							
Smoking habit of husband	8155	107					
Never	1505	13	21 926	1.00	(reference)	1.00	(reference)
Former	2570	28	37 302	1.28	(0.66, 2.47)	1.24	(0.64, 2.40)
Current (0 < to 20 cigarettes/day)	2478	37	36 446	1.71	(0.91, 3.21)	1.67	(0.89, 3.14)
Current (≥21 cigarettes/day)	1602	29	23 658	2.03	(1.05, 3.93)	1.98	(1.03, 3.84)
Trend <i>P</i>				0.021		0.023	

†Estimated hazard ratio after adjustments for age, body mass index (quartiles), physical activity score, alcohol consumption, education years (≤8, 9–11, 12–14, ≥15 years), age at menarche (≤12, 13–14, 15–16, ≥17 years), age at first delivery (non-parous, ≤20, 21–25, 26–30, ≥31 years), menopausal status (premenopausal, postmenopausal ≤49 years, postmenopausal ≥50 years), parity number (0, 1, 2, ≥3) and history of hormone replacement therapy (yes, no). HR, hazard ratio.

Table 3. Associations of husband's smoking status with incidence of breast cancer according to menopausal status and alcohol consumption at baseline among never smokers

	Husband's smoking status				Trend <i>P</i>
	Never	Former	Current (0 < to 20 cigarettes/day)	Current (≥21 cigarettes/day)	
<i>Menopausal status at baseline</i>					
<i>Premenopausal</i>					
Number of subjects	737	970	1189	1052	
Incidence	7	9	16	18	
Person-years	10 940	14 497	17 741	15 635	
Multivariate-adjusted HR†	1.00 (reference)	0.92 (0.34–2.49)	1.34 (0.55–3.27)	1.67 (0.69–4.02)	0.11
<i>Postmenopausal</i>					
Number of subjects	745	1568	1261	539	
Incidence	6	19	21	11	
Person-years	10 642	22 367	18 299	7859	
Multivariate-adjusted HR‡	1.00 (reference)	1.51 (0.60–3.80)	1.97 (0.79–4.89)	2.18 (0.80–5.95)	0.13
<i>Alcohol consumption at baseline</i>					
<i>Non-drinkers (alcohol consumption =0 g/day)</i>					
Number of subjects	448	833	754	461	
Incidence	2	8	12	10	
Person-years	6419	11 765	10 850	6679	
Multivariate-adjusted HR§	1.00 (reference)	1.97 (0.41–9.42)	3.34 (0.74–14.98)	5.29 (1.14–24.54)	0.011
<i>Drinkers (alcohol consumption >0 g/day)</i>					
Number of subjects	1057	1737	1724	1141	
Incidence	11	20	25	19	
Person-years	15 508	25 537	25 596	16 979	
Multivariate-adjusted HR¶	1.00 (reference)	1.06 (0.51–2.23)	1.33 (0.65–2.71)	1.43 (0.68–3.02)	0.25

†Estimated hazard ratio after adjustments for age, body mass index (quartiles), physical activity score, alcohol consumption, education years (≤8, 9–11, 12–14y, ≥15 years), age at menarche (≤12, 13–14, 15–16 ≥17 years), age at first delivery (non-parous, ≤20, 21–25, 26–30, ≥31 years), parity number (0, 1, 2, ≥3) and history of hormone replacement therapy (yes, no). ‡Estimated hazard ratio after adjustments for age, body mass index, physical activity score, alcohol consumption, education years, age at menarche, age at menopause (≤49, ≥50 years), age at first delivery, parity number and history of hormone replacement therapy. §Estimated hazard ratio after adjustments for age, body mass index, physical activity score, education years, age at menarche, age at first delivery, menopausal status (premenopausal, postmenopausal ≤49 years, postmenopausal ≥50 years), parity number, and history of hormone replacement therapy. ¶Estimated hazard ratio after adjustments for age, body mass index, physical activity score, alcohol consumption, education years, age at menarche, age at first delivery, menopausal status, parity number and history of hormone replacement therapy.

(Table 3). Among postmenopausal never smokers, women whose husband was a current smoker of 21 cigarettes per day or more had a relative risk of 2.18 (95% CI: 0.80–5.95) for breast cancer compared with women with a husband who had never smoked.

The analyses stratified by alcohol consumption among never smokers revealed that the increased risks of breast cancer among women having smoking husband were stronger among those who consumed no alcohol, although the interaction was not statistically significant (*P* for interaction = 0.51). We repeated stratified analysis using the median alcohol intake (1.48 g/day) as a cut-off value. Among non-drinkers and light-drinkers (alcohol intake ≤1.48 g/day), the hazard ratios for breast cancer were 2.94 (95% CI: 0.85–10.14), 4.14 (95% CI: 1.24–13.86) and 4.94 (95% CI: 1.42–17.25), respectively, for women whose husband was a former smoker, a current smoker of 20 cigarettes per day or less, and a current smoker of 21 cigarettes per day or more, compared with women whose husband had never smoked. Among drinkers (alcohol intake >1.48 g/day), the corresponding values were 0.71 (95% CI: 0.30–1.67), 0.95 (95% CI: 0.43–2.12) and 1.19 (95% CI: 0.52–2.70), respectively. The *P*-value for interaction by alcohol drinking was 0.18.

We re-analyzed the data after excluding 12 patients who were diagnosed with breast cancer in the first 2 years of follow up to eliminate those who might have had breast cancer but

had not noticed it yet at baseline. None of the results were substantially altered.

Discussion

Previous reports about smoking and breast cancer have mainly consisted of US and European studies, and there have been few studies on the Asian population.^(20–25) To our knowledge, there are only five prospective Japanese cohorts that reported the association of active^(20–23) and passive smoking^(20,22–24) with breast cancer, and they showed conflicting results. Only one study⁽²²⁾ reported a positive association between active smoking and breast cancer incidence; the other three studies reported null association.^(20,21,23) For passive smoking, one study revealed the increased risk for breast cancer mortality among postmenopausal nonsmoking women,⁽²⁰⁾ and another showed the risk increment of incidence among premenopausal women.⁽²²⁾ Meanwhile, null⁽²³⁾ and negative⁽²⁴⁾ associations were also reported.

In this study, we observed an increased risk of breast cancer among women who were exposed to cigarette smoke from their husbands, and the risk increment showed a dose-response relationship with the number of cigarettes. A stronger positive relationship between a husband's smoking and breast cancer was observed among women who did not habitually consume alcohol. Active smoking was not associated with the risk of breast cancer.

Active smoking has been reported to have simultaneously opposite effects on the progress of breast cancer; some smoke constituents, such as polycyclic aromatic hydrocarbons, aromatic amines and N-nitrosamines, potentially induce mammary carcinogenesis, while the antiestrogenic effects of smoking reduce the risk of breast cancer.^(7,14) Although these factors might complicate a relationship between active smoking and breast cancer risk, our results regarding active smoking might have been influenced by the fact that the smoking rate of women in this generation was very low, so that it is difficult to meaningfully evaluate the effect of active smoking on breast cancer in this cohort. In addition, it is likely that Japanese female smokers concealed their smoking. The reference group might be irrelevant to truly smoke-free persons; it included never smokers who were exposed to secondhand smoke. However, the analyses of women without husbands smoking did not have enough statistical power to find any associations ($N = 1607$). Further evidence is needed on the association between active smoking and breast cancer.

Sidestream smoke has been reported to contain chemical compounds, including some carcinogens.⁽⁹⁾ Some of the carcinogens are metabolized and activated by mammary epithelial cells.⁽²⁶⁾ A higher prevalence of smoking-specific DNA adducts and p53 mutation was reported in smokers than in non-smokers.^(27,28) Our results support the theory that there is a carcinogenic property of tobacco smoke for breast cancer, by demonstrating the association between husbands smoking and increased risk of breast cancer with a dose-response relationship. Compared with previous US and European studies, the risks of breast cancer were estimated to be at a higher level, consistent with another Japanese study by Hirayama,⁽²⁰⁾ showing that the relative risk for breast cancer mortality was 1.3 among women whose husband smoked 1–19 cigarettes daily and 2.68 among those whose husband smoked 20 cigarettes or more daily. However, we also must note that we did not detect risk increment of breast cancer among active smokers who inhale sidestream smoke through their own smoking.

We additionally observed that an increased risk of breast cancer among women with a smoking husband was pronounced among those who did not habitually consume alcohol. Although our finding suggests that non-drinkers were susceptible to the effect tobacco smoke has on breast cancer, the analyses were conducted with a small number of cases in subgroup analyses, showing the possibility that the results were obtained by chance. Two previous case-control studies^(29,30) and one cohort study⁽¹⁰⁾ reported that alcohol consumption did not modify the association with breast cancer, which is inconsistent with our results. However, all three studies observed an overall null association between passive smoking and breast cancer, whereas we detected a significant positive association between husbands smoking and breast cancer risk. For active smoking, it was observed in a Norwegian–Swedish cohort study that the risks from active smoking were estimated to be higher among non-drinkers than among all subjects.⁽³¹⁾

Mechanisms underlying the associations between smoking, alcohol and breast cancer are unknown. Because alcohol has been hypothesized to affect breast cancer by increasing estrogen levels,⁽¹²⁾ the small difference in circulating estrogen or alcohol levels might influence cigarette smoke's carcinogenic property. Slow acetylation of aromatic amines was related to an increased risk of breast cancer.⁽⁵⁾ Although there might be a greater proportion of women with N-acetyltransferase 2 (NAT2) slow genotype among non-drinkers, the association between NAT2 genotypes and drinking habits is not well

known. With the increasing evidence of an association between DNA methylation and breast cancer,⁽³²⁾ smoking and drinking might be involved in DNA methylation changes by interfering with each other. The modifying effects of alcohol on increased breast cancer risk from passive smoking might need to be confirmed in future studies.

Our cohort study was conducted with a prospective design which is expected to be less subject to bias than a case-control study because the information on smoking status was collected before the diagnosis of breast cancer. In addition, we estimated alcohol consumption using a validated semi-quantitative FFQ. The other strengths of our study were a good participation rate, a long follow up and information obtained for several confounders.

Our study has several limitations that warrant consideration. Information on subjects' or husbands' smoking status was based on self-reports. Compared with estimates based on urinary cotinine concentration, high sensitivity and specificity of self-reported smoking status were reported (92.1 and 98.4% for men, and 91.2 and 98.3% for women).⁽³³⁾ However, in the present study, husbands' smoking status was obtained only for the subjects whose spouse was ascertained from the study data (67.4%). When 3681 women who reported being single, widowed or divorced at the baseline were assigned to the group without exposure to smoke from a husband, the positive association between husband's smoking and breast cancer was not altered. Compared with the reference group of women with a husband who had never smoked or who were without a husband, the hazard ratio was 1.76 (95% CI: 1.11–2.79) among women whose husband was a current smoker of 21 cigarettes per day or more. Passive smoking except for smoke exposure from the subjects' husbands was not assessed; none of the exposure to smoke from other residents at home, at the workplace or in public places was obtained. The exposure evaluation was performed only at baseline and included no information on smoking exposure during childhood. Changes in smoking or alcohol habits during the follow-up period were unknown. Although underlying diseases or preclinical signs at the baseline may have affected lifestyles, the exclusion of those who had died during the first 2 years of follow up did not substantially change the results. Finally, despite the consideration of numerous lifestyle, reproductive and dietary factors in the analyses, we might not have fully excluded some residual or unknown confounding of lifestyle or social factors.

In conclusion, this prospective study of Japanese women demonstrated the increased risk of breast cancer among women exposed to secondhand cigarette smoke from their husband, with a dose-response relationship. The increased risks for women with a smoking husband were stronger among those who do not habitually consume alcohol. These results suggest that exposure to smoke from husbands is a potential risk factor for breast cancer, and, considering the limited data currently available, the modifying effects of alcohol on increased breast cancer risk from passive smoking need to be confirmed in further studies.

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Disclosure Statement

The authors have no conflict of interest to declare.

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