RESEARCH ARTICLE

Cigarette Smoking and Breast Cancer: a Case-control Study in Serbia

Milena Ilic[1]*, Hristina Vlajinac[2], Jelena Marinkovic[3]

Abstract

Background: Despite the fact that breast cancer is the most common female cancer worldwide, more than half of the breast cancer risk factors remained unexplained. The aim of this study was to investigate the association of cigarette smoking with risk of breast cancer. Materials and Methods: A case-control study was conducted in the Clinical Centre of Kragujevac, Serbia, covering 382 participants (191 cases and 191 controls). In the analysis of data logistic regression was used. Results: Breast cancer risk was significantly increased in those who quit smoking at ≤50 years of age (OR=2.72; 95% confidence interval - 95%CI=1.02-7.27) and in those who quit smoking less than 5 years before diagnosis of the disease (OR=4.36; 95%CI=1.12-16.88). When smokers were compared with nonsmokers without passive exposure to smoking, former smoking significantly increased breast cancer risk (OR=2.37; 95%CI=1.07-5.24). Risk for breast cancer was significantly increased in those who quit smoking at ≤50 years of age (OR=3.29; 95%CI=1.17-9.27) and in those who quit smoking less than 5 years before diagnosis of the disease (OR=5.46; 95%CI=1.34-22.28). Conclusions: These data suggest that cigarette smoking is associated with an elevated risk of breast cancer among former smokers in Serbia.

Keywords: Smoking - breast cancer - risk factor - case-control study - Serbia

Asian Pac J Cancer Prev, **14 (11)**, 6643-6647

Introduction

Despite the fact that breast cancer is the most common female cancer worldwide, more than half of the breast cancer risk factors remained unexplained (Madigan et al., 1995; Rockhill et al., 1998; Jemal et al, 2011). Smoking as one of the postulated risk factors for breast cancer has been a subject of numerous studies, because it is one of the few factors that could be modified (Hamajima et al., 2002; Gaudet et al., 2013; Hartz and He, 2013; Pirie et al., 2013).

Results of numerous epidemiological studies about the relationship between cigarette smoking and breast cancer risk are inconsistent (International Agency for Research on Cancer, 2004; Braithwaite et al., 2012). The majority of studies have shown a weak positive association (Reynolds et al., 2004; Cui et al., 2006; Rollison et al., 2008; Slattery et al., 2008; Young et al., 2009) or absence of any association (Prescott et al., 2007; Roddam et al., 2007; Lin et al., 2008; Trivers et al., 2009). In some studies even inverse association was found (Gammon et al., 1998; Lash and Aschengrau, 2002). Some studies suggested that an increased risk of breast cancer may be associated with long duration of tobacco use (Conlon et al., 2010; Bjerkaas et al, 2013; McKenzie et al., 2013), or high intensity of smoking (Cui et al., 2006; Conlon et al., 2010; Luo et al., 2011), early age at smoking initiation (Magnusson et al., 2007; Luo et al., 2011), smoking at least 5 years before first full-term pregnancy (Reynolds et al., 2004) and decreasing years since quitting (Gram et al., 2005; Young et al., 2009).

The results concerning the relationship between passive smoking (environmental tobacco smoke) and breast cancer risk have been more consistent (Lee and Hamling, 2006; Johnson et al., 2011; Reynolds et al., 2009; Gao et al., 2013). While the results from some studies are unconvincing (Pirie et al., 2008; Anderson et al., 2012), the numerous studies suggested an increase in risk with exposure to passive tobacco smoke (Kropp and Chang-Claude, 2002; Slattery et al., 2008; Luo et al., 2011). This association has been stronger for premenopausal compared to postmenopausal women (Hanaoka et al., 2005; Slattery et al., 2008). The purpose of this study was to investigate the association between cigarette smoking and breast cancer risk.

Materials and Methods

Case-control study was conducted in Clinical Centre of Kragujevac (town in central Serbia with about 200,000 inhabitants) between January 2004 and December 2005, and comprised overall 382 participants.

Case group consisted of 191 patients with newly diagnosed and histologically confirmed breast cancer: no one refused to participate. The mean time interval between diagnosis and interview of cases was 2 months.

*[1]Department of Epidemiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, [2]Institute of Epidemiology, [3]Institute of Medical Statistics and Informatics, Faculty of Medicine, University of Belgrade, Belgrade, Serbia *For correspondence: drmilenailic@yahoo.com*

The controls (191 participants), individually matched by age (+/-2 years), hospital admittance and place of residence (rural or urban) to the respective case, were selected from a female patients admitted because of other diseases to Clinical Centre Kragujevac, and had neither diagnostic nor anamnestic data for breast cancer. The most frequent diagnosis among the controls were injuries, chronic rheumatic diseases, cholecystitis, hernia, etc.

In-person interviews were conducted using a structured questionnaire. Data were collected on demographic characteristics, reproductive history, smoking and alcohol consumption, personal history of some chronic diseases and family history of breast cancer. In the present paper are presented data on smoking. Information on cigarette smoking included: active smoking status (never smokers, former and current smokers), the passive exposure among never smokers, smoking intensity (average number of cigarettes smoked per day: ≤10, 11-20, ≥21), duration of smoking (total number of smoking years: <20, 20-29, ≥30), age of smoking initiation (≥20, <20), smoking before first full-term pregnancy (<5 years and ≥5 years) and among former smokers, age when they stopped smoking (≤50, >50) and years since quitting smoking (>5, ≤5). A smoker was defined as a woman who had smoked at least 1 cigarette per day during 1 year at any time in life. A former smoker was defined as a woman who stopped smoking with abstinence duration of at least one year from quitting smoking. Passive smoking included household and/or occupation passive smoking exposure. With regard to passive smoking exposure, never smokers were divided into those with and without passive exposure. Women were classified as pre-/perimenopausal if they reported having menstrual periods within the one year before the interview. Postmenopausal women were those in whom menstrual periods ceased more than a year ago due to either natural or artificial menopause. The interviews were always conducted in the hospital (on admission, after operation or after control examination). The interview took approximately two hours. Oral informed consent was obtained from all study participants before interview.

In the statistical analysis, chi-square test, Fisher's exact test and logistic regression method were applied. In order to estimate the association between cigarette smoking and breast cancer risk, odds ratio (OR) with 95% confidence intervals (95%CI) was calculated. All ORs were adjusted for variables known, from literature data, as possible confounders for association between smoking habits and breast cancer: educational level, marital status, age at menarche, menopausal status, breastfeeding history, family history of breast cancer, body mass index and alcohol consumption. Cardiovascular disease in personal medical history was added as possible confounder since it was significantly more frequently reported by controls then cases. Age, occupation, parity and abortion history were not included in the multivariate models because of their collinearity with some of the former variables. A two-tailed probability value of $p<0.050$ was considered significant.

Table 1. Baseline Demographic Characteristics of Women with Breast Cancer and Their Controls

		Cases (N=191) No	%	Controls (N=191) No	%	p*
Age groups	≤40	7	3.7	6	3.1	
	41-50	32	16.8	31	16.2	
	51-60	67	35.1	66	34.6	
	61-70	61	31.9	60	31.4	
	>70	24	12.6	28	14.7	0.981
Occupation†	Clerks, craftsman	46	24.1	56	29.3	
	Manual workers, farmers, housewives	145	75.9	135	70.7	0.247
Educational level	Incomplete primary	81	42.4	77	40.3	
	Primary	44	23	39	20.4	
	Secondary	50	26.2	57	29.8	
	Higher	16	8.4	18	9.4	0.454
Marital status	With partner	122	63.9	136	71.2	
	Without partner‡	69	36.1	55	28.8	0.127

*p: probability value (according to Chi-Square Tests and Fisher's Exact Test) indicates statistical significance of the differences in cases and controls; †For pensioner, occupation before retirement; ‡Never married, widowed, divorced

Table 2. Smoking Status of Cases with Breast Cancer and Their Controls

Active smoking history		Cases (N=191) No	%	Controls (N=191) No	%	Odds ratio (95% confidence intervals) Unadjusted	Adjusted*
		Passive smokers† included in reference category					
Active smoking status	Never smokers	130	68.1	124	64.9	1.00 (referent)	1.00 (referent)
	Ever smokers	61	31.9	67	35.1	0.87 (0.57-1.33)	0.93 (0.57-1.51)
	Former smokers	25	13.1	13	6.8	1.83 (0.90-3.75)	2.12 (0.98-4.59)
	Current smokers	36	18.8	54	28.3	0.64 (0.39-1.04)	0.65 (0.38-1.13)
Smoking intensity	≤10	20	10.5	19	9.9	1.00 (0.51-1.97)	1.20 (0.57-2.50)
(No. of cigarettes smoked per day)	11-20	31	16.2	36	18.8	0.82 (0.48-1.41)	0.85 (0.47-1.53)
	≥21	10	5.2	12	6.3	0.79 (0.33-1.91)	0.79 (0.30-2.05)
Total No. of smoking years	<20	22	11.5	9	4.7	2.33 (1.03-5.26)	2.31 (0.97-5.53)
	20-29	19	9.9	24	12.6	0.76 (0.39-1.45)	0.90 (0.43-1.87)
	≥30	20	10.5	34	17.8	0.56 (0.31-1.03)	0.59 (0.30-1.13)
Age of smoking initiation	<20	15	7.9	23	12.0	0.62 (0.31-1.23)	0.56 (0.25-1.25)
	≥20	46	24.1	44	23.0	1.00 (0.62-1.61)	1.10 (0.65-1.86)
Years of smoking before first birth‡	<5	17	11.8	18	12.6	0.89 (0.44-1.81)	0.99 (0.44-2.23)
	≥5	9	6.3	14	9.8	0.60 (0.25-1.45)	0.56 (0.21-1.50)
Age stopped smoking‖	≤50	18	11.6	7	5.1	2.45 (0.99-6.10)	2.72 (1.02-7.27)
	>50	7	4.5	6	4.4	1.11 (0.36-3.40)	1.68 (0.51-5.59)
Years since quitting smoking‖	≤5	12	7.7	10	7.3	1.14 (0.48-2.74)	1.57 (0.61-4.07)
	>5	13	8.4	3	2.2	4.13 (1.15-14.85)	4.36 (1.12-16.88)

*Multivariate model was adjusted for educational level, marital status, age at menarche, menopausal status, breastfeeding history, family history of breast cancer, body mass index, alcohol use, and cardiovascular disease in personal medical history; †Household and occupation passive smoking exposure; ‡Nulliparous women were excluded from the analysis; ‖ Only former smokers

All statistical analyses were conducted using the Statistical Package for Social Sciences software (SPSS Inc., version 19.0, Chicago, IL).

Results

Majority of participants (79.6% of cases and 80.7% of controls) were 50 and more years old. Incomplete or complete primary school had 65.4% of cases and 60.7% of controls. About three quarters (75.9% of cases and 70.7% of controls) were manual workers, farmers or housewives and 63.9% of cases and 71.2% of controls lived with partner (Table 1). Postmenopausal were 80.6% of cases and 84.8% of controls.

When passive smokers were included in the reference category, according to adjusted odds ratios (OR), cases and controls did not significantly differ in smoking habit (either current smoker or former smoker), number of cigarettes smoked per day, duration of smoking, age of smoking initiation and smoking before first full-term pregnancy (Table 2). In former smokers adjusted risk for breast cancer was significantly increased in those who quit smoking at ≤50 years of age (OR=2.72; 95% confidence interval – 95%CI=1.02-7.27) and in those who quit smoking less than 5 years before diagnosis of the disease (OR=4.36; 95% CI=1.12-16.88).

When smokers were compared with nonsmokers without passive exposure to smoking (Table 3), former smoking significantly increased breast cancer risk (OR=2.37; 95%CI=1.07-5.24). Women who smoked less than 20 years were at higher risk than those who smoked longer (OR=2.48, 95%CI=1.01-6.06). Risk for breast cancer was significantly increased in those who quit smoking at ≤50 years of age (OR=3.29; 95%CI=1.17-9.27) and in those who quit smoking less than 5 years before diagnosis of the disease (OR=5.46; 95%CI=1.34-22.28). In never smokers who were exposed to passive smoking, breast cancer risk was higher than in those not exposed to passive smoking, but this difference was not significant.

Discussion

In the present study breast cancer was associated with former smoking but only in comparison with never smokers without passive exposure to smoking. Breast cancer risk was significantly increased in women who quite smoking at age ≤50 years, and in those who quite smoking before more than 5 years.

As already stated, data about relationship between breast cancer and smoking are inconsistent. In the year 2002, Collaborative Group on Hormonal Factors and Breast Cancer, after reanalysis of over 80% of the worldwide epidemiological data on breast cancer and tobacco consumption, concluded that smoking was not associated with breast cancer (Hamajima et al., 2002).

However, on the basis of the review of studies among Japanese women, Nagata et al. (2006) concluded that tobacco smoking possibly increases the risk for breast cancer. They could not explain the differences between Japanese and non-Japanese women by differences in the number of cigarettes smoked or the number of years of smoking, nor by differences in endogenous estrogen status or distribution of certain genes related to metabolic enzymes.

In the many large cohort studies reported after the year 2000 (Reynolds et al., 2004; Cui et al., 2006; Luo et al., 2011; Xue et al., 2011), although not in all of them (Lin et al., 2008; Ahern et al., 2009; Brown et al., 2010), both active and passive smoking were found to be associated with an increase in breast cancer. A Canadian Expert Panel has reviewed new studies of this subject since 2002 (Johnson et al., 2011). Based on the weight of evidence from these epidemiological and toxicological studies

Table 3. Tobacco Exposure of Cases with Breast Cancer and Their Controls

Active smoking history		Cases (N=191) No	%	Controls (N=191) No	%	Odds ratio (95% confidence intervals) Unadjusted	Adjusted*
		Passive smokers† excluded from reference category					
Active smoking history							
Never smokers without passive exposure		98	51.3	102	53.4	1.00 (referent)	1.00 (referent)
Never smokers with passive exposure		32	16.8	22	11.5	1.51 (0.82-2.78)	1.57 (0.81-3.03)
Ever smokers		61	31.9	67	35.1	0.95 (0.61-1.48)	1.01 (0.60-1.70)
Former smokers		25	13.1	13	6.8	2.00 (0.97-4.13)	2.37 (1.07-5.24)
Current smokers		36	18.8	54	28.3	0.69 (0.42-1.15)	0.72 (0.40-1.27)
Smoking intensity	≤10	20	12.6	19	11.2	1.10 (0.55-2.18)	1.27 (0.60-2.71)
(No. of cigarettes smoked per day)	11-20	31	19.5	36	21.3	0.90 (0.51-1.56)	0.94 (0.50-1.76)
	≥21	10	6.3	12	7.1	0.87 (0.36-2.10)	0.81 (0.31-2.17)
Total No. of smoking years	<20	22	13.8	9	5.3	2.54 (1.12-5.79)	2.48 (1.01-6.06)^
	20-29	19	11.9	24	14.2	0.82 (0.42-1.69)	1.02 (0.47-2.19)
	≥30	20	12.6	34	20.1	0.61 (0.33-1.14)	0.65 (0.33-1.27)
Age of smoking initiation	<20	15	9.4	23	13.6	0.68 (0.33-1.38)	0.61 (0.27-1.42)
	≥20	46	28.9	44	26	1.09 (0.66-1.79)	1.17 (0.67-2.05)
Years of smoking before first birth‡	<5	17	14.8	18	14.6	0.97 (0.47-1.99)	1.02 (0.43-2.40)
	≥5	9	7.8	14	11.4	0.66 (0.27-1.60)	0.58 (0.21-1.62)
Age stopped smoking‖	≤50	18	14.6	7	6.1	2.67 (1.07-6.68)	3.29 (1.17-9.27)
	>50	7	5.7	6	5.2	1.21 (0.39-3.74)	1.74 (0.53-7.76)
Years since quitting smoking‖	≤5	12	9.8	10	8.7	1.25 (0.52-3.02)	1.73 (0.66-4.55)
	>5	13	10.6	3	2.6	4.51 (1.25-16.31)	5.46 (1.34-22.28)

*Multivariate model was adjusted for educational level, marital status, age at menarche, menopausal status, breastfeeding history, family history of breast cancer, body mass index, alcohol use, and cardiovascular disease in personal medical history; †Household and occupation passive smoking exposure; ^After adjusting for "Years since quitting smoking", the association was not significant (OR 8.93, 95%CI 0.77-103.51); ‡Nulliparous women were excluded from the analysis; ‖ Only former smokers

and on understanding of biological mechanisms, they concluded that the association between active smoking and breast cancer is consistent with causality as well as the association between passive smoking and breast cancer among younger, primarily premenopausal women (Johnson et al., 2011).

In the present study current smoking was not associated with breast cancer. This could be explained by the fact that the study is small and that its statistical power was not enough to reveal weak or modest increase in the risk of breast cancer. The findings that former smokers were at increased risk for breast cancer is in line with results from some other investigations showing that breast cancer risk is higher in former that in current smokers (Manjer et al., 2000; Manjer et al., 2004; Saquib et al., 2013). Tobacco smoke contains chemicals, which are carcinogenic to humans and can cause mammary tumors in animals (Chen et al., 2011). At the same time smoking can reduce breast cancer risk through its antiestrogenic effect (Band et al., 2002). It has been suggested that antiestrogenic effect is present only in current smokers and that it disappears after quitting smoking. In the study of Manjer et al. (2004), former smoking was associated with postmenopausal breast cancer in women with high level of estrogens (estrone or estradiol). It is supposed that after smoking cessation a rebound effect regarding estrogen levels causes the elevation of breast cancer risk, which gradually decreased and returns to base-line after about 20 years (Manjer et al., 2004; Li et al., 2005; Luo et al., 2011). However, in some other studies (Reynolds et al., 2004; Cui et al., 2006) the relationship between years since quitting smoking and breast cancer risk was not found. In the present study, the risk for breast cancer was higher in women who quit smoking before more that 5 years than in women whose period from smoking cessation was shorter. Although some explanations for such finding could be speculated, as individual variation in the reversal of the antiestrogenic effect after cessation of smoking (Manjer et al., 2004), or differences in the frequency of estrogen receptors-positive and estrogen receptors –negative breast cancer, there is no possibility to confirm any of them (Kabat et al., 2011). Data on passive smoking were not detailed enough to investigate its effect on breast cancer risk. However, the fact that former smoking increased breast cancer risk only in comparison with never smokers who were not exposed to passive smoking, in an indirect way suggests that passive smoking could be related to breast cancer. The finding of the present study that breast cancer risk was higher in those who smoked less than 20 years than in those who smoked longer, was the most probable the result of a significant association of duration of smoking and age at cessation of smoking ($p<0.001$). Those who quit smoking at age of 50 or less years had shorter duration of smoking. After adjustment for age at smoking cessation, breast cancer risk in those who smoked less than 20 years was not significant (OR 8.93, 95%CI 0.77-103.51). Besides drawbacks incorporated in case-control design, the main limitation of the present study is a small number of participants.

In conclusion, the present study breast cancer risk was increased in former smokers, especially those who quit smoking at age of 50 or less years, and in those who quite smoking before more than 5 years. The risk was not increased in current smokers and was not related to age of smoking initiation, smoking before first full-pregnancy, intensity and duration of smoking. Further studies investigating genetic and hormonal characteristics and their impact on the effect of smoking on breast cancer risk could help our understanding of this association.

Acknowledgements

This work was supported by the Ministry of Education and Science of Republic of Serbia, through Contract No. 175042.

References

Ahern TP, Lash TL, Egan KM, Baron JA (2009). Lifetime tobacco smoke exposure and breast cancer incidence. *Cancer Causes Control,* **20**, 1837-44.

Anderson LN, Cotterchio M, Mirea L, Ozcelik H, Kreiger N (2012). Passive cigarette smoke exposure during various periods of life, genetic variants, and breast cancer risk among never smokers. *Am J Epidemiol*, **175**, 289-301.

Band PR, Le ND, Fang R, Deschamps M (2002). Carcinogenic and endocrine disrupting effects of cigarette smoke and risk of breast cancer. *Lancet*, **360**, 1044-9.

Bjerkaas E, Parajuli R, Weiderpass E, et al (2013). Smoking duration before first childbirth: an emerging risk factor for breast cancer? Results from 302,865 Norwegian women. *Cancer Causes Control*, **24**, 1347-56.

Braithwaite D, Izano M, Moore DH, et al (2012). Smoking and survival after breast cancer diagnosis: a prospective observational study and systematic review. *Breast Cancer Res Treat*, **136**, 521-33.

Brown LM, Gridley G, Wu AH, et al (2010). Low level alcohol intake, cigarette smoking and risk of breast cancer in Asian-American women. *Breast Cancer Res Treat*, **120**, 203-10.

Chen CS, Lee CH, Hsieh CD, et al (2011). Nicotine-induced human breast cancer cell proliferation attenuated by garcinol through down-regulation of the nicotinic receptor and cyclin D3 proteins. *Breast Cancer Res Treat*, **125**, 73-87.

Conlon MS, Johnson KC, Bewick MA, Lafrenie RM, Donner A (2010). Smoking (active and passive), N-acetyltransferase 2, and risk of breast cancer. *Cancer Epidemiol*, **34**, 142-9.

Cui Y, Miller AB, Rohan TE (2006). Cigarette smoking and breast cancer risk: pdate of a prospective cohort study. *Breast Cancer Res Treat*, **100**, 293-9.

Gammon MD, Schoenberg JB, Teitelbaum SL, et al (1998). Cigarette smoking and breast cancer risk among young women (United States). *Cancer Causes Control*, **9**, 583-90.

Gao CM, Ding JH, Li SP, et al (2013). Active and passive smoking, and alcohol drinking and breast cancer risk in chinese women. *Asian Pac J Cancer Prev*, **14**, 993-6.

Gaudet MM, Gapstur SM, Sun J, et al (2013). Active smoking and breast cancer risk: original cohort data and meta-analysis. *J Natl Cancer Inst*, **105**, 515-25.

Gram IT, Braaten T, Terry PD, et al (2005). Breast cancer risk among women who start smoking as teenagers. *Cancer Epidemiol Biomarkers Prev*, **14**, 61-6.

Hamajima N, Hirose K, Tajima K, et al (2002). Alcohol, tobacco and breast cancer - Collaborative reanalysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the disease. *Br J Cancer*, **87**, 1234-45.

Hanaoka T, Yamamoto S, Sobue T, Sasaki S, Tsugane S (2005).

Active and passive smoking and breast cancer risk in middle-aged Japanese women. *Int J Cancer*, **114**, 317-22.

Hartz AJ, He T (2013). Cohort study of risk factors for breast cancer in post menopausal women. *Epidemiol Health*, **35**, 2013003.

International Agency for Research on Cancer. IARC Monographs on the evaluation of carcinogenic risks to humans: Tobacco smoke and involuntary smoking. Vol. 83. Lyon, France: IARC; 2004.

Jemal A, Bray F, Center MM, et al (2011). Global cancer statistics. *CA Cancer J Clin*, **61**, 69-90.

Johnson KC, Miller AB, Collishaw NE, et al (2011). Active smoking and secondhand smoke increase breast cancer risk: the report of the canadian expert panel on tobacco smoke and breast cancer risk (2009). *Tob Control*, **20**, 2.

Kabat GC, Kim M, Phipps AI, et al (2011). Smoking and alcohol consumption in relation to risk of triple-negative breast cancer in a cohort of postmenopausal women. *Cancer Causes Control*, **22**, 775-83.

Kropp S, Chang-Claude J (2002). Active and passive smoking and risk of breast cancer by age 50 years among German women. *Am J Epidemiol*, **156**, 616-26.

Lash TL, Aschengrau A (2002). A null association between active or passive cigarette smoking and breast cancer risk. *Breast Cancer Res Treat*, **75**, 181-4.

Lee PN, Hamling J (2006). Environmental tobacco smoke exposure and risk of breast cancer in nonsmoking women: a review with meta-analyses. *Inhal Toxicol*, **18**, 1053-70.

Li CI, Malone KE, Daling JR (2005). The relationship between various measures of cigarette smoking and risk of breast cancer among older women 65-79 tears of age. *Cancer Causes Control*, **16**, 975-85.

Lin Y, Kikuchi S, Tamakoshi K, et al (2008). Active smoking, passive smoking, and breast cancer risk: findings from the Japan collaborative cohort study for evaluation of cancer risk. *J Epidemiol*, **18**, 77-83.

Luo J, Margolis KL, Wactawski-Wende J, et al (2011). Association of active and passivesmoking with risk of breast cancer among postmenopausal women: a prospective cohort study. *BMJ*, **342**, 1016.

McKenzie F, Ellison-Loschmann L, Jeffreys M, et al (2013). Cigarette smoking and risk of breast cancer in a New Zealand multi-ethnic case-control study. *PLoS One*, **8**, 63132.

Magnusson C, Wedren S, Rosenberg LU (2007). Cigarette smoking and breast cancer risk: a population-based study in Sweden. *Br J Cancer*, **97**, 1287-90.

Madigan MP, Ziegler RG, Benichou J, Byrne C, Hoover RN (1995). Proportion of breast cancer cases in the United States explained by well-established risk factors. *J Natl Cancer Inst*, **87**, 1681-5.

Manjer J, Berglund G, Bondesson L, et al (2000). Breast cancer incidence in relation to smoking cessation. *Breast Cancer Res Treat*, **61**, 121-9.

Manjer J, Johansson R, Lenner P (2004). Smoking is associated with postmenopausal breast cancer in women with high levels of estrogen. *Int J Cancer*, **112**, 324-8.

Nagata C, Mizoue T, Tanaka K, et al (2006). Tobacco smoking and breast cancer risk: an evaluation based on a systematic review of epidemiological evidence among the Japanese population. *Jpn J Clin Oncol*, **36**, 387-94.

Pirie K, Beral V, Peto R, et al (2008). Passive smoking and breast cancer in never smokers: prospective study and meta-analysis. *Int J Epidemiol*, **37**, 1069-79.

Pirie K, Peto R, Reeves GK, Green J, Beral V (2013). The 21st century hazards of smoking and benefits of stopping: a prospective study of one million women in the UK. *Lancet*, **381**, 133-41.

Prescott J, Ma H, Bernstein L, Ursin G (2007). Cigarette smoking is not associated with breast cancer risk in young women. *Cancer Epidemiol Biomarkers Prev*, **16**, 620-2.

Reynolds P, Goldberg D, Hurley S, et al (2009). Passive smoking and risk of breast cancer in the California teachers study. *Cancer Epidemiol Biomarkers Prev*, **18**, 3389-98.

Reynolds P, Hurley S, Goldberg DE, et al (2004). Active smoking, household passive smoking, and breast cancer: evidence from the California Teachers Study. J *Natl Cancer Inst*, **96**, 29-37.

Rockhill B, Weinberg CR, Newman B (1998). Population attributable fraction estimation for established breast cancer risk factors: considering the issues of high prevalence an unmodifiability. *Am J Epidemiol*, **147**, 826-33.

Roddam AW, Pirie K, Pike MC, et al (2007). Active and passive smoking and the risk of breast cancer in women aged 36-45 years: a population based case-control study in the UK. *Br J Cancer*, **97**, 434-9.

Rollison DE, Brownson RC, Hathcock HL, Newschaffer CJ (2008). Case-control study of tobacco smoke exposure and breast cancer risk in Delaware. *BMC Cancer*, **8**, 157.

Saquib N, Stefanick ML, Natarajan L, Pierce JP (2013). Mortality risk in former smokers with breast cancer: Pack-years vs. smoking status. *Int J Cancer*, **133**, 2493-7.

Slattery ML, Curtin K, Giuliano AR, et al (2008). Active and passive smoking, IL6, ESR1, and breast cancer risk. *Breast Cancer Res Treat*, **109**, 101-11.

Trivers KF, Lund MJ, Porter PL, et al (2009). The epidemiology of triple-negative breast cancer, including race. *Cancer Causes Control*, **20**, 1071-82.

Xue F, Willett WC, Rosner BA, Hankinson SE, Michels KB (2011). Cigarette smoking and the incidence of breast cancer. *Arch Intern Med*, **171**, 125-33.

Young E, Leatherdale S, Sloan M, et al (2009). Age of smoking initiation and risk of breast cancer in a sample of Ontario women. *Tob Induc Dis*, **5**, 4.