

Contents of Supplemental Materials

Supplemental Table 1. Description of cohort studies that contributed to the pooled analysis of active cigarette smoking and invasive breast cancer risk among 14 cohorts in the National Cancer Institute Cohort Consortium

Supplemental Table 2. Multivariable-adjusted hazard ratios (HR) and 95% confidence intervals (CI) of the association of risk factors with invasive breast cancer risk, a pooled analysis among 14 cohorts in the NCI Cohort Consortium

Supplemental Table 3a. Multivariable-adjusted associations of invasive breast cancer risk with smoking characteristics stratified by age at first birth, a pooled analysis among 14 cohorts in the National Cancer Institute Cohort Consortium

Supplemental Table 3b. Multivariable-adjusted associations of smoking characteristics with invasive breast cancer risk stratified by smoking duration in ever smokers, a pooled analysis among 14 cohorts in the National Cancer Institute Cohort Consortium

Supplemental Table 4. Multivariable-adjusted hazard ratios (HR) and 95% confidence intervals (CI) for the association of smoking characteristics with invasive breast cancer risk by menopausal status and age at menopause, a pooled analysis among 14 cohorts in the NCI Cohort Consortium

Supplemental Figure 1. Forest plot of hazard ratios (HR) and 95% confidence intervals (CI) for the risk of breast cancer associated with current (A.) and former (B.) smoking in comparison to never smoking in 14 cohorts in the National Cancer Institute Cohort Consortium

Supplemental Figure 2. Forest plot of hazard ratios (HR) and 95% confidence intervals (CI) for the risk of breast cancer associated with smoking initiation prior to first birth (A.) and smoking initiation after first birth (B.) in comparison to never smoking in 14 cohorts in the National Cancer Institute Cohort Consortium

Supplemental Table 1. Description of cohort studies that contributed to the pooled analysis of active cigarette smoking and invasive breast cancer risk among 14 cohorts in the National Cancer Institute Cohort Consortium.

Study Name (Acronym)	Year of Questionnaire	Median Follow-up Time (years)	Total N	Case N	Age at Questionnaire Mean (SD)	Post-menopausal %	Never smoker %	Age at smoking initiation ¹ Mean (SD)	Smoking initiation prior to first birth %	Non-Drinker %	Obese ² %	First-degree family history %	ER+ cases ³ %	Distant stage cases ³ %
Agricultural Health Study (AHS)	1993-1997	15.0	30,788	1,078	47.4 (12.7)	26.9	71.7	19.5 (5.3)	5.3	44.5	16.3	11.2	65.1	3.4
Cancer Prevention Study-II (CPSII)	1992-1993	15.8	73,384	4,217	62.1 (6.5)	94.4	56.2	19.4 (5.0)	33.4	46.0	15.4	14.0	65.2	1.8
Iowa Women's Health Study (IWHHS)	1986	22.9	37,051	2,803	61.6 (4.2)	98.8	65.9	21.9 (7.0)	21.1	50.9	23.5	11.8	73.1	3.4
Melbourne Collaborative Cohort Study (MCCS)	1990-1994	17.4	23,135	1,074	54.5 (8.6)	64.0	69.3	20.5 (6.6)	20.9	42.4	22.0	N/A	71.5	N/A
NIH-AARP Diet and Health Study (AARP)	2004-2006	2.1	98,346	955	69.0 (5.4)	100.0	50.0	19.8 (5.6)	36.6	N/A	21.9	14.5	68.6	0.8
Nurses' Health Study (NHS)	1980	27.4	85,489	6,881	46.2 (7.2)	32.8	44.1	19.5 (3.7)	49.8	32.1	11.1	6.7	65.7	1.8
Nurses' Health Study 2 (NHS2)	1989-1990	19.4	114,518	2,480	34.4 (4.7)	6.2	65.1	18.6 (3.3)	22.8	37.9	11.1	2.0	67.1	0.6
Norwegian Women and Cancer Study (NOWAC)	1991-2008	12.9	165,458	3,964	49.4 (8.5)	36.2	34.7	18.6 (5.2)	51.0	27.5	8.2	5.3	51.0	2.8
Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO)	1993-2001	8.9	68,483	3,043	62.5 (5.4)	99.7	56.4	19.6 (5.6)	32.8	22.0	24.6	13.8	79.7	1.6
Singapore Chinese Health Study (SCHS)	1993-1999	12.5	34,028	670	56.2 (8)	71.8	91.3	22.3 (7.2)	4.1	90.9	3.5	1.3	40.8	N/A
Swedish Mammography Cohort (SMC)	1997	14.1	36,467	1,438	61.5 (9.2)	91.0	53.9	19.9 (6.4)	33.3	17.3	10.5	9.0	79.6	N/A
Swedish Women's Lifestyle and Health Study (SWLH)	1991-1992	21.0	48,779	1,824	39.2 (5.8)	N/A	40.7	17.7 (3.9)	48.9	6.9	5.6	16.8	67.6	N/A
Vitamins And Lifestyle Study (VITAL)	2000-2002	9.9	37,020	1,457	61.2 (7.5)	91.9	55.7	19.2 (3.8)	30.8	43.8	23.9	15.0	60.0	2.8
Women's Health Initiative Observational Study (WHI-OS)	1993-1997	11.9	81,735	4,176	63.5 (7.3)	100.0	51.2	20.2 (5.2)	32.7	29.7	24.4	17.9	77.2	1.2

¹ Among ever smokers. ² Obesity is defined as a body mass index (kg/m²) of 30.0 or higher. ³ Calculated among cases with available data. Note: N/A, not available

Supplemental Table 2. Multivariable-adjusted* hazard ratios (HR) and 95% confidence intervals (CI) of the association of risk factors with invasive breast cancer risk, a pooled analysis among 14 cohorts in the NCI Cohort Consortium

	Cases	Multivariable-adjusted*		p-value
		HR	95% CI	
Parity				
Nulliparous	4,224	1.00		
Parous	31,413	0.83	(0.80, 0.86)	9.4E-29
Missing	423	0.96	(0.81, 1.15)	0.67
Family history of breast cancer				
No	26,411	1.00		
Yes	5,258	1.48	(1.43, 1.52)	7.0E-136
Missing	4,391	1.01	(0.97, 1.05)	0.67
History of benign breast disease				
No	15,933	1.00		
Yes	7,178	1.35	(1.31, 1.39)	9.9E-94
Missing	12,949	1.13	(0.97, 1.33)	0.12
Ever use of oral contraceptives				
Never	18,619	1.00		
Ever	16,827	1.02	(1.00, 1.04)	0.11
Missing	614	0.96	(0.85, 1.08)	0.51
Ever use of HRT				
Never	20,940	1.00		
Ever	13,678	1.13	(1.10, 1.16)	4.8E-20
Missing	1,442	1.03	(0.96, 1.10)	0.44
Body mass index (kg/m²)				
<18.5	484	1.00		
18.5-22.4	9,560	1.18	(1.08, 1.29)	4.3E-04
22.5-24.9	8,886	1.20	(1.09, 1.31)	1.2E-04
25-29.9	10,506	1.24	(1.13, 1.35)	5.7E-06
≥30	5,927	1.35	(1.23, 1.48)	2.5E-10
Missing	697	1.17	(1.04, 1.31)	0.01
Alcohol consumption				
Non-current drinker	11,404	1.00		
<1 drink/day	17,521	1.05	(1.03, 1.08)	3.4E-05
2 drinks/day	3,081	1.20	(1.15, 1.25)	4.5E-17
3+ drinks/day	1,248	1.36	(1.28, 1.44)	8.7E-24
Missing	2,806	0.93	(0.88, 0.99)	0.01

* Multivariable-adjusted models included age, cohort, race/ ethnicity, education, birth year, family history of breast cancer, history of benign breast disease, ever use of oral contraceptives, menopausal status and age at menopause, age at menarche, ever use of menopausal hormone therapy, number of live births, body mass index, and amount and frequency of alcohol use.

Supplemental Table 3a. Multivariable-adjusted* associations of invasive breast cancer risk with smoking characteristics stratified by age at first birth, a pooled analysis among 14 cohorts in the National Cancer Institute Cohort Consortium

Smoking initiation relative to first birth in parous women	Age at First Birth									p-value for interaction
	<25			25-29			30+			
	Cases	HR	95% CI	Cases	HR	95% CI	Cases	HR	95% CI	
Never Smoker	9010	1.00		4712	1.00		2042	1.00		
Started after first birth	1553	1.08	(1.02, 1.14)	181	0.98	(0.85, 1.14)	33	1.10	(0.78, 1.55)	
≤5 years before first birth	4934	1.08	(1.04, 1.12)	908	1.06	(0.99, 1.14)	71	0.92	(0.73, 1.17)	
6-10 years before first birth	2412	1.13	(1.08, 1.19)	2368	1.07	(1.02, 1.12)	421	1.07	(0.96, 1.19)	
>10 years before first birth	42	1.10	(0.81, 1.49)	707	1.14	(1.05, 1.23)	1316	1.07	(0.99, 1.14)	0.51
P-trend			0.12			0.02			0.28	

* Multivariable-adjusted models included age, cohort, race/ ethnicity, education, birth year, family history of breast cancer, history of benign breast disease, ever use of oral contraceptives, menopausal status and age at menopause, age at menarche, ever use of menopausal hormone therapy, number of live births, body mass index, and amount and frequency of alcohol use.

Supplemental Table 3b. Multivariable-adjusted* associations of smoking characteristics with invasive breast cancer risk stratified by smoking duration in ever smokers, a pooled analysis among 14 cohorts in the National Cancer Institute Cohort Consortium

Smoking initiation relative to first birth in parous, ever smoking women	Smoking Duration in Ever Smokers												p-value for interaction
	<10 years			10-19 years			20-39 years			40+ years			
	Cases	RR [†]	95% CI	Cases	RR [†]	95% CI	Cases	RR [†]	95% CI	Cases	RR [†]	95% CI	
Started after first birth	374	1.00		415	1.00		818	1.00		128	1.00		
≤5 years before first birth	897	1.04	(0.92, 1.17)	1321	1.08	(0.96, 1.21)	2937	0.97	(0.89, 1.05)	692	0.96	(0.79, 1.16)	
6-10 years before first birth	854	1.08	(0.96, 1.23)	1235	1.16	(1.03, 1.29)	2396	1.03	(0.95, 1.12)	628	1.00	(0.82, 1.21)	
>10 years before first birth	285	1.29	(1.10, 1.51)	614	1.23	(1.08, 1.41)	916	1.21	(1.09, 1.34)	234	1.11	(0.89, 1.39)	0.74
P-trend			0.23			0.048			3x10 ⁻³			0.36	

* Multivariable-adjusted models included age, cohort, race/ ethnicity, education, birth year, family history of breast cancer, history of benign breast disease, ever use of oral contraceptives, menopausal status and age at menopause, age at menarche, ever use of menopausal hormone therapy, age at first birth and number of live births, body mass index, and amount and frequency of alcohol use.

Table 4. Multivariate-adjusted* hazard ratios (HR) and 95% confidence intervals (CI) for the association of smoking characteristics with invasive breast cancer risk by menopausal status and age at menopause, a pooled analysis among 14 cohorts in the NCI Cohort Consortium

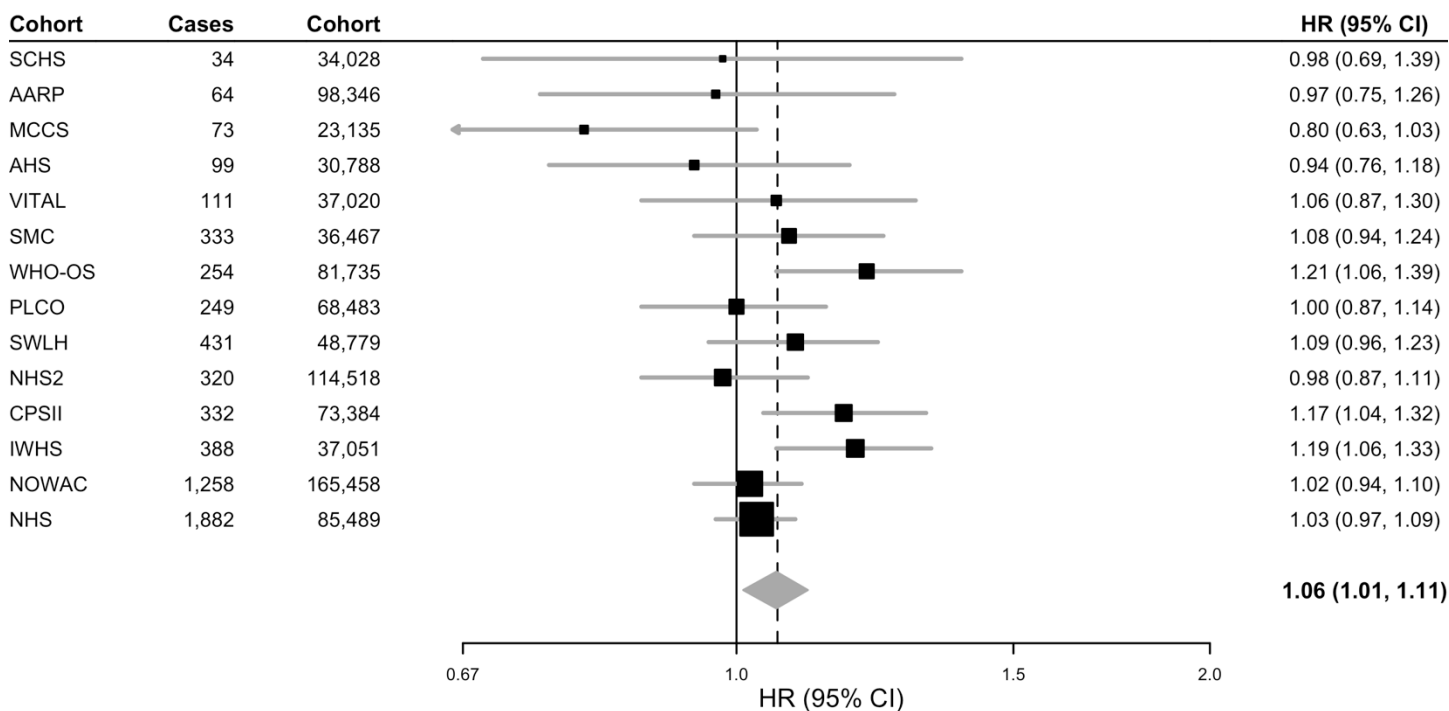
	Not menopausal			Menopausal at <50			Menopausal at 50-54			Menopausal at ≥55			p-values for interaction
	Cases	HR	95% CI	Cases	HR	95% CI	Cases	HR	95% CI	Cases	HR	95% CI	
Smoking Status													
Never smoker	5,095	1.00		4,962	1.00		5,198	1.00		1,435	1.00		0.50
Former smoker	2,929	1.01	(0.97, 1.06)	3,364	1.07	(1.02, 1.12)	3,092	1.09	(1.04, 1.14)	761	1.06	(0.97, 1.16)	
Current smoker	2,447	1.06	(1.01, 1.12)	1,459	1.07	(1.01, 1.14)	1,077	1.07	(1.00, 1.14)	158	1.07	(0.90, 1.26)	
Cigarettes per day in current smokers													
Never smoker	5,095	1.00		4,962	1.00		5,198	1.00		1,435	1.00		0.76
<10	485	1.06	(0.96, 1.16)	275	1.05	(0.92, 1.18)	256	1.17	(1.03, 1.33)	37	0.97	(0.70, 1.34)	
10-19	810	1.08	(1.00, 1.16)	481	1.06	(0.97, 1.17)	340	1.04	(0.93, 1.16)	57	1.11	(0.85, 1.45)	
20-29	694	1.02	(0.94, 1.10)	457	1.12	(1.01, 1.23)	286	0.99	(0.88, 1.12)	45	1.24	(0.92, 1.67)	
30-39	284	1.11	(0.98, 1.25)	154	1.12	(0.96, 1.32)	98	1.01	(0.83, 1.24)	13	1.15	(0.67, 1.99)	
≥40	157	1.24	(1.06, 1.46)	77	1.04	(0.83, 1.30)	55	1.27	(0.97, 1.65)	3	0.81	(0.26, 2.52)	
p-value for linear trend [†]			0.04			0.09			0.77			0.33	
Years of smoking in current smokers													
Never smoker	5,095	1.00		4,962	1.00		5,198	1.00		1,435	1.00		2x10 ⁻⁴
<10 years	50	0.82	(0.62, 1.09)	18	1.28	(0.81, 2.04)	11	1.11	(0.61, 2.00)	1	1.03	(0.15, 7.32)	
10-19 years	649	1.14	(1.05, 1.25)	36	0.83	(0.6, 1.16)	12	0.74	(0.42, 1.30)	2	0.80	(0.20, 3.20)	
20-39 years	1,702	1.07	(1.01, 1.14)	815	1.02	(0.94, 1.10)	582	1.04	(0.96, 1.14)	52	1.06	(0.81, 1.41)	
40+ years	26	0.47	(0.32, 0.70)	571	1.17	(1.08, 1.28)	458	1.11	(1.01, 1.22)	103	1.10	(0.90, 1.34)	
p-value for linear trend [†]			0.52			1x10 ⁻³			0.02			0.60	
Years of smoking in former smokers													
Never smoker	5,095	1.00		4,962	1.00		5,198	1.00		1,435	1.00		0.97
<5	724	1.05	(0.97, 1.13)	305	0.94	(0.84, 1.06)	313	1.03	(0.92, 1.16)	69	0.91	(0.71, 1.16)	
5-10	563	1.00	(0.91, 1.09)	339	1.04	(0.93, 1.16)	346	1.07	(0.96, 1.19)	90	0.99	(0.80, 1.23)	
10-20	1,026	1.06	(0.99, 1.13)	825	1.10	(1.02, 1.19)	785	1.13	(1.04, 1.21)	185	1.04	(0.89, 1.22)	
20-30	361	1.04	(0.93, 1.16)	779	1.06	(0.98, 1.14)	681	1.07	(0.98, 1.15)	165	1.06	(0.90, 1.25)	
30-40	92	1.00	(0.81, 1.23)	661	1.12	(1.03, 1.22)	583	1.10	(1.01, 1.20)	142	1.15	(0.97, 1.37)	
>40	10	0.86	(0.46, 1.61)	241	1.17	(1.03, 1.33)	206	1.22	(1.06, 1.40)	52	1.13	(0.86, 1.49)	
p-value for linear trend [†]			0.10			6x10 ⁻³			0.13			0.09	
Years since quitting in former smokers													
Never smoker	5,095	1.00		4,962	1.00		5,198	1.00		1,435	1.00		
≥31	378	0.96	(0.86, 1.07)	749	1.05	(0.97, 1.13)	725	1.05	(0.97, 1.13)	186	1.01	(0.87, 1.18)	
21-30	1,082	0.99	(0.93, 1.06)	879	1.07	(1.00, 1.15)	778	1.10	(1.02, 1.19)	179	1.08	(0.93, 1.26)	
11-20	1,351	1.08	(1.02, 1.15)	964	1.10	(1.03, 1.18)	792	1.16	(1.07, 1.25)	169	1.23	(1.05, 1.44)	

1-10	2,447	1.06	(1.01, 1.11)	1,459	1.07	(1.01, 1.14)	1,077	1.07	(1.00, 1.14)	158	1.07	(0.90, 1.26)	0.66
p-value for linear trend [†]			0.01			0.26			0.04			0.03	
Age at initiation in ever smokers													
Never smoker	5,095	1.00		4,962	1.00		5,198	1.00		1,435	1.00		
<16	450	0.98	(0.89, 1.08)	441	1.05	(0.95, 1.15)	353	1.10	(0.99, 1.23)	77	1.10	(0.99, 1.23)	
16-20	3,391	1.04	(0.99, 1.08)	2,766	1.10	(1.04, 1.15)	2,333	1.08	(1.03, 1.13)	497	1.08	(1.03, 1.13)	
21-25	1,242	1.10	(1.04, 1.18)	1,086	1.08	(1.01, 1.16)	982	1.10	(1.03, 1.18)	214	1.10	(1.03, 1.18)	
≥25	240	0.96	(0.84, 1.10)	351	0.96	(0.87, 1.06)	426	1.04	(0.94, 1.15)	112	1.04	(0.94, 1.15)	0.50
p-value for linear trend [†]			0.81			0.03			0.25			0.64	
Smoking initiation relative to first birth in parous ever smokers													
Never smoker	4,276	1.00		4,327	1.00		4,623	1.00		1,312	1.00		
After first birth	341	1.14	(0.94, 1.39)	592	0.88	(0.72, 1.06)	522	1.06	(0.88, 1.29)	115	1.06	(0.86, 1.32)	
≤5 years before birth	1,909	1.18	(0.97, 1.43)	1,708	0.95	(0.78, 1.17)	1,365	1.10	(0.90, 1.35)	295	1.34	(1.03, 1.75)	
6-10 years before birth	1,661	1.30	(1.06, 1.59)	1,354	0.78	(0.65, 0.94)	1,311	0.92	(0.77, 1.11)	279	1.03	(0.85, 1.24)	
>10 years before birth	767	1.12	(0.92, 1.35)	435	1.12	(0.90, 1.40)	455	0.78	(0.64, 0.96)	102	1.02	(0.84, 1.25)	0.50
p-value for linear trend [†]			3x10 ⁻⁴			6x10 ⁻⁴			0.01			0.04	

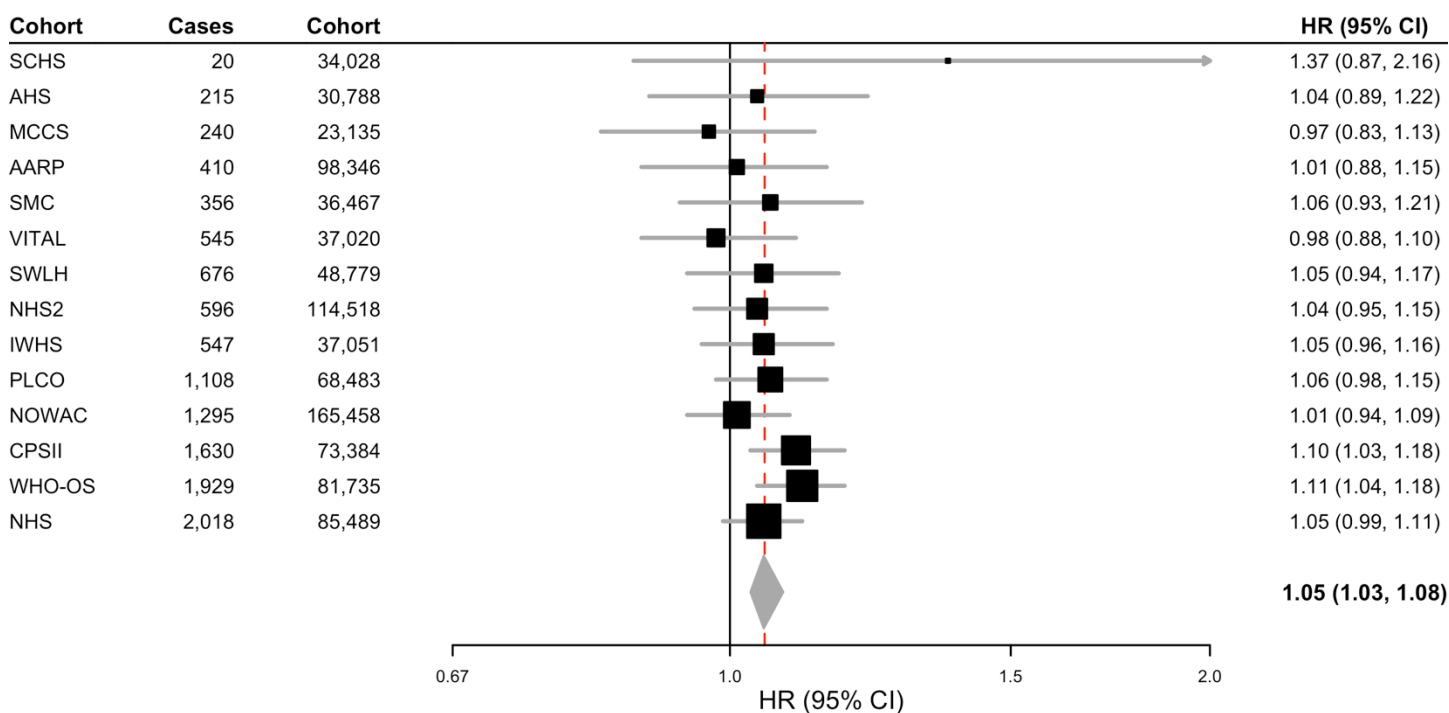
*Multivariable-adjusted models included age, cohort, race/ ethnicity, education, birth year, family history of breast cancer, history of benign breast disease, ever use of oral contraceptives, menopausal status and age at menopause, age at menarche, ever use of menopausal hormone therapy, age at first birth and number of live births, body mass index, and amount of alcohol use. †Linear trend was evaluated using a continuous version of the variable excluding never smokers.

Supplemental Figure 1. Forest plot of hazard ratios (HR) and 95% confidence intervals (CI) for the risk of breast cancer associated with current (A.) and former (B.) smoking in comparison to never smoking in 14 cohorts in the National Cancer Institute Cohort Consortium. Study abbreviation (defined in Supplemental Table 1) and sample size of exposed cases and total cohort are provided. Estimates are weighted and ranked according to the inverse of the variance of the log HR estimate. HRs are represented by squares (size is proportional to the aforementioned weights) and CIs are represented by the error bars. The solid vertical line represents the null value and the dotted vertical line represents the overall summary estimate.

A. Current vs never smoking

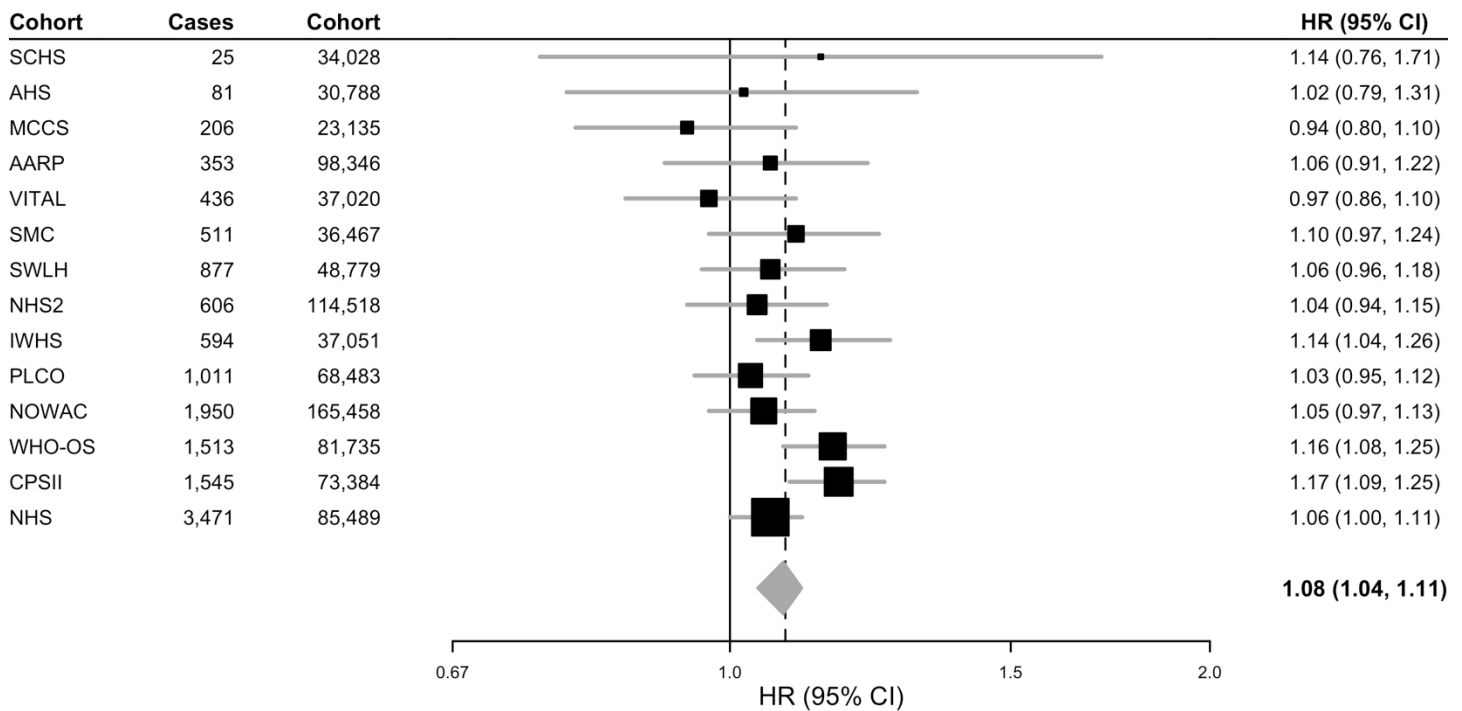


B. Former vs never smoking



Supplemental Figure 2. Forest plot of hazard ratios (HR) and 95% confidence intervals (CI) for the risk of breast cancer associated with smoking initiation prior to first birth (A.) and smoking initiation after first birth (B.) in comparison to never smoking in 14 cohorts in the National Cancer Institute Cohort Consortium. Study abbreviation (defined in Supplemental Table 1) and sample size of exposed cases and total cohort are provided. Estimates weighted and ranked according to the inverse of the variance of the log HR estimate. HRs are represented by squares (size is proportional to the aforementioned weights) and CIs are represented by the error bars. The solid vertical line represents the null value and the dotted vertical line represents the overall summary estimate.

A. Smoking initiation before first birth



B. Smoking initiation after first birth

