

WEB APPENDIX

Smoking Assessment

In the study questionnaire, ever smoking tobacco was defined as ever having smoked the equivalent of at least 1 cigarette every 1–3 days for at least 6 months. Among ever smokers, information was collected on ages at smoking initiation and cessation and average number of cigarettes or cigarette equivalents smoked per day. Cigarette equivalents were one-quarter of a cigar or 1 gram of tobacco in a hand-rolled cigarette, water pipe, dry pipe, or other form of smoking tobacco. Because of the low frequency of smoking tobacco in forms other than cigarettes (among male controls, 1,218 [64%] had smoked cigarettes, 404 [21%] had smoked hand-rolled cigarettes, 9 [0.5%] had smoked water pipes, 3 [0.2%] had smoked dry pipes, none smoked cigars, and 1 [0.05%] had smoked another form of tobacco), we combined all forms of tobacco for analysis. Average intensity of smoking was calculated as the duration-weighted average of all types of tobacco smoked. Total duration of smoking was calculated as latest age at cessation (for former smokers) or age at diagnosis or interview (for currently smoking cases or controls, respectively) minus earliest age at initiation. Time since smoking cessation for former smokers was calculated as age at diagnosis or interview (for cases or controls, respectively) minus latest age at cessation. Pack-years of smoking was calculated as total duration times average number of cigarette equivalents smoked per day, divided by 20 cigarettes per pack. Information was also collected on whether subjects smoked filtered or unfiltered cigarettes and whether they engaged in deep inhalation.

To reduce the influence of reverse causation among cases, i.e., smoking cessation due to NPC symptoms or diagnosis, current smokers were classified as those who reported currently smoking or having quit within the last 3 years; former smokers were classified as cases who had quit at least 4 years prior to diagnosis. Among controls, reverse causation was not a concern; however, to allow for a lag period after smoking cessation, current smokers were classified as those who had smoked within the last year before interview, and former smokers were classified as those who had quit at least 2 years prior to interview.

Based on cutoffs used in prior studies and observed distributions among study controls, age at smoking initiation was categorized as <20, 20–<30, or ≥30 years. Smoking intensity was categorized as <10, 10–<20, 20–<30, or ≥30 cigarettes per day. Smoking duration was categorized as <10, 10–<20, 20–<30, or ≥30 years. Time since smoking cessation was categorized as 4–<10 years (cases)/2–<10 years (controls) or ≥10 years. Cumulative smoking was categorized as <10, 10–<20, 20–<30, or ≥30 pack-years.

Questions on passive smoking separately evaluated childhood and adulthood residential exposure to passive smoking, including separate questions on the subject's relationship to each smoking relative and the smoking duration and intensity of each relative; and workplace exposure to passive smoking, including separate questions on daily duration and total duration of workplace passive smoking. Total intensity of residential passive smoking was calculated based on the sum of each relative's daily number of cigarettes smoked, and duration of residential passive smoking was calculated based on the longest smoking duration of any relative. Cumulative residential passive smoking exposure was calculated based on the sum of each relative's pack-years of smoking (intensity times duration), while cumulative workplace passive smoking exposure was calculated based on the product of daily duration times total duration of exposure.

Residential passive smoking exposure in childhood or adulthood was categorized as ever or never, with additional classification of ever-exposed subjects by number of smoking relatives (1 or ≥2), relation of smoking relative(s), combined passive smoking intensity (<10, 10–<20, or ≥20 cigarettes/day), longest passive smoking duration (<10 or ≥10 years for childhood; <10, 10–<20, or ≥20 years for adulthood), and cumulative passive smoking (<10, 10–<20, or ≥20 pack-years) in either childhood or adulthood.

Workplace passive smoking exposure was categorized as ever or never, with additional classification of ever-exposed subjects by daily passive smoking duration (<30, 30–<60, 60–<120, or ≥120 minutes) or total passive smoking duration (<10, 10–<20, or ≥20 years).

Web Table 1. Exposure Frequencies and Odds Ratios (ORs) With 95% Confidence Intervals (CIs) for Associations Between Active Smoking and Risk of Nasopharyngeal Carcinoma Among Men, Stratified by Use of Filtered and/or Unfiltered Cigarettes, Guangdong Province and Guangxi Autonomous Region, China, 2010–2014

Exposure	Category	Unfiltered Cigarettes Only				Filtered Cigarettes Only				Filtered and Unfiltered Cigarettes				<i>P</i> _{homogeneity} ^b
		Cases, <i>n</i>	Controls, <i>n</i>	OR ^a	95% CI ^a	Cases, <i>n</i>	Controls, <i>n</i>	OR ^a	95% CI ^a	Cases, <i>n</i>	Controls, <i>n</i>	OR ^a	95% CI ^a	
Smoking status														
	Never ^c	462	544	1.00	Referent	462	544	1.00	Referent	462	544	1.00	Referent	
	Former	20	39	0.74	0.42, 1.30	122	151	0.96	0.73, 1.27	37	52	1.05	0.67, 1.65	
	Current	134	119	1.56	1.15, 2.11	784	790	1.16	0.99, 1.36	298	212	1.94	1.55, 2.44	0.01
Age at smoking initiation (years)														
	< 20	70	68	1.41	0.97, 2.04	424	334	1.47	1.21, 1.78	177	142	1.72	1.32, 2.24	
	20–< 30	71	66	1.50	1.02, 2.20	380	466	0.96	0.79, 1.15	140	101	1.96	1.45, 2.64	
	≥ 30	13	24	0.77	0.38, 1.55	90	136	0.81	0.60, 1.08	18	21	1.36	0.70, 2.63	0.15
No. of cigarettes smoked per day														
	< 10	125	124	1.41	1.03, 1.93	93	136	0.81	0.60, 1.08	127	97	1.87	1.37, 2.53	
	10–< 20	16	16	1.36	0.66, 2.77	194	249	0.90	0.72, 1.13	162	127	1.77	1.35, 2.33	
	20–< 30	9	13	0.94	0.39, 2.24	465	439	1.25	1.04, 1.49	33	27	1.75	1.02, 2.98	
	≥ 30	4	5	1.19	0.31, 4.51	141	112	1.51	1.14, 2.00	13	13	1.38	0.63, 3.03	0.09
Duration of smoking (years)														
	< 10	6	8	0.92	0.32, 2.70	85	87	1.02	0.73, 1.42	8	4	2.36	0.70, 7.93	
	10–< 20	8	13	0.80	0.32, 1.96	189	227	0.89	0.70, 1.12	30	17	1.96	1.06, 3.62	
	20–< 30	26	25	1.26	0.71, 2.24	318	314	1.17	0.96, 1.43	90	54	2.04	1.42, 2.93	
	≥ 30	114	112	1.52	1.09, 2.11	301	308	1.31	1.05, 1.63	207	189	1.63	1.26, 2.12	0.46
Time since smoking cessation (years) ^d														
	4 (cases) or 2 (controls)–<10	8	24	0.47	0.21, 1.07	46	94	0.58	0.40, 0.84	15	32	0.67	0.35, 1.27	
	≥ 10	12	15	1.18	0.54, 2.59	66	57	1.42	0.97, 2.08	22	20	1.68	0.89, 3.17	0.03

Pack-years of smoking													
< 10	126	127	1.37	1.01, 1.86	183	223	0.90	0.71, 1.14	60	34	2.36	1.51, 3.69	
10-< 20	11	9	1.61	0.66, 3.94	189	221	0.95	0.76, 1.20	70	55	1.67	1.14, 2.45	
20-< 30	8	5	2.12	0.68, 6.58	213	228	1.10	0.88, 1.38	72	65	1.51	1.05, 2.17	
≥ 30	9	17	0.80	0.35, 1.84	308	264	1.51	1.22, 1.87	133	110	1.83	1.35, 2.47	0.06

^a Adjusted for age and geographic area.

^b Tests of homogeneity were conducted among ever smokers.

^c All never smokers were the reference group for all comparisons.

^d Current smokers were included in the analysis as a separate category, but are not shown here.

Web Table 2. Exposure Frequencies and Odds Ratios (ORs) With 95% Confidence Intervals (CIs) for Associations Between Active Smoking and Risk of Nasopharyngeal Carcinoma Among Men, Stratified by Deep Inhalation, Guangdong Province and Guangxi Autonomous Region, China, 2010–2014

Exposure	Category	Deep Inhalation				Not Deep Inhalation				$P_{\text{homogeneity}}^b$
		Cases, <i>n</i>	Controls, <i>n</i>	OR ^a	95% CI ^a	Cases, <i>n</i>	Controls, <i>n</i>	OR ^a	95% CI ^a	
Smoking status										
	Never ^c	462	544	1.00	Referent	462	544	1.00	Referent	
	Former	98	120	1.01	0.75, 1.37	81	122	0.85	0.62, 1.16	
	Current	726	583	1.50	1.27, 1.78	490	538	1.09	0.91, 1.30	0.70
Age at smoking initiation (years)										
	<20	427	332	1.54	1.27, 1.87	244	212	1.38	1.10, 1.73	
	20–<30	346	310	1.36	1.11, 1.66	245	323	0.91	0.74, 1.12	
	≥30	51	61	1.10	0.74, 1.64	70	120	0.71	0.51, 0.99	0.13
No. of cigarettes smoked per day										
	<10	182	166	1.48	1.15, 1.91	163	191	0.99	0.77, 1.28	
	10–<20	236	212	1.34	1.07, 1.68	136	180	0.91	0.70, 1.18	
	20–<30	295	247	1.38	1.12, 1.71	212	232	1.14	0.91, 1.43	
	≥30	110	78	1.67	1.21, 2.30	48	52	1.14	0.75, 1.73	0.91
Duration of smoking (years)										
	<10	62	37	1.79	1.16, 2.76	37	62	0.64	0.42, 0.99	
	10–<20	129	125	1.07	0.80, 1.42	98	132	0.83	0.62, 1.11	
	20–<30	256	209	1.39	1.11, 1.74	178	184	1.14	0.90, 1.45	
	≥30	376	332	1.60	1.29, 1.99	246	277	1.22	0.96, 1.55	0.06

Time since smoking cessation (years) ^d									
<10 [4 (cases) or 2 (controls)]	37	70	0.65	0.42, 0.99	32	80	0.51	0.33, 0.78	
≥10	61	50	1.55	1.03, 2.32	39	42	1.21	0.76, 1.92	0.95
Pack-years of smoking									
<10	197	165	1.52	1.19, 1.94	172	219	0.90	0.71, 1.14	
10–<20	164	154	1.21	0.94, 1.57	106	131	0.97	0.73, 1.29	
20–<30	182	165	1.28	1.00, 1.64	111	133	1.03	0.77, 1.37	
≥30	280	219	1.66	1.32, 2.09	170	172	1.31	1.01, 1.69	0.38

^a Adjusted for age and geographic area.

^b Tests of homogeneity were conducted among ever smokers.

^c All never smokers were the reference group for all comparisons.

^d Current smokers were included in the analysis as a separate category, but are not shown here.

Web Table 3. Odds Ratios (ORs)^a With 95% Confidence Intervals (CIs) for Associations Between Cross-Classified Smoking Duration and Age at Initiation With Risk of Nasopharyngeal Carcinoma Among Ever Smoking Men (with Never Smokers as Referent), Guangdong Province and Guangxi Autonomous Region, China, 2010–2014

Duration of Smoking (years)	Age at Smoking Initiation (years)			
	0 (Referent)	<20 OR; 95% CI	20–<30 OR; 95% CI	≥30 OR; 95% CI
0	1.00	---	---	---
<10	---	1.08; 0.59, 1.97	1.21; 0.70, 2.08	0.74; 0.46, 1.18
10–<20	---	0.84; 0.58, 1.23	1.03; 0.77, 1.37	0.75; 0.48, 1.17
20–<30	---	1.52; 1.18, 1.96	1.13; 0.89, 1.42	1.12; 0.70, 1.78
≥30	---	1.66; 1.34, 2.05	1.18; 0.93, 1.51	0.89; 0.48, 1.65

^a Adjusted for age, geographic area, and time since smoking cessation.

Web Table 4. Odds Ratios (ORs)^a With 95% Confidence Intervals (CIs) for Associations Between Active Smoking Characteristics Classified as Continuous Variables and Risk of Nasopharyngeal Carcinoma Among Men, Guangdong Province and Guangxi Autonomous Region, China, 2010–2014

Exposure	OR ^a	95% CI ^a
Model 1: Intensity, duration, and time since cessation		
Intensity (per 10 cigarettes/day)	1.016	0.949, 1.088
Duration (per year)	1.010	1.005, 1.016
Time since cessation (per year)	1.018	1.003, 1.034
Model 2: Intensity, age at initiation, and time since cessation		
Intensity (per 10 cigarettes/day)	1.049	0.974, 1.131
Age at initiation (per year)	0.969	0.957, 0.980
Time since cessation (per year)	1.010	0.994, 1.025
Model 3: Cumulative exposure, duration, and time since cessation		
Cumulative (per 10 pack-years)	1.050	1.005, 1.097
Duration (per year)	1.007	1.001, 1.013
Time since cessation (per year)	1.019	1.003, 1.034

^a Adjusted for age, geographic area, and other smoking characteristics shown.

Web Table 5. Exposure Frequencies and Odds Ratios (ORs) With 95% Confidence Intervals (CIs) for Associations Between Passive Smoking and Risk of Nasopharyngeal Carcinoma Among Never Smoking Women, Guangdong Province and Guangxi Autonomous Region, China, 2010–2014

Exposure Category	Cases, <i>n</i>	Controls, <i>n</i>	OR ^a	95% CI ^a	<i>P</i> _{trend} ^a	OR ^b	95% CI ^b	<i>P</i> _{trend} ^b	OR ^c	95% CI ^c
Passive smoking at residence in childhood										
No ^d	245	278	1.00	Referent		1.00	Referent		1.00	Referent
Yes	415	391	1.18	0.94, 1.48		1.17	0.93, 1.48		1.14	0.90, 1.33
No. of smoking relatives in childhood										
1	365	338	1.20	0.96, 1.51		1.20	0.95, 1.53			
≥2	50	53	1.03	0.67, 1.57	0.32	0.97	0.62, 1.52	0.43		
Relation of smoking relative(s) in childhood										
Parent	394	367	1.20	0.96, 1.50		1.20	0.94, 1.51			
Sibling	33	41	0.87	0.53, 1.42		0.74	0.43, 1.25			
Other	18	15	1.32	0.65, 2.71		1.40	0.65, 3.02			
Combined intensity of passive smoking in childhood (cigarettes per day)										
<10	80	73	1.21	0.84, 1.74		1.22	0.84, 1.79			
10-<20	121	136	1.00	0.74, 1.35		1.00	0.73, 1.37			
≥20	177	173	1.13	0.86, 1.50	0.46	1.10	0.82, 1.47	0.66		
Longest duration of passive smoking in childhood (years)										
<10	17	13	1.42	0.68, 3.00		1.43	0.66, 3.10			
≥10	398	378	1.17	0.94, 1.47	0.19	1.16	0.92, 1.47	0.24		
Cumulative passive smoking in childhood (pack-years)										
<10	179	188	1.06	0.81, 1.38		1.07	0.80, 1.42			
10-<20	162	163	1.11	0.84, 1.46		1.09	0.81, 1.46			
≥20	37	31	1.33	0.79, 2.21	0.26	1.21	0.71, 2.07	0.45		
Passive smoking at residence in adulthood										
No ^e	193	228	1.00	Referent		1.00	Referent			
Yes	467	441	1.27	1.01, 1.60		1.20	0.94, 1.53			

No. of smoking relatives in adulthood									
1	364	357	1.22	0.96, 1.55		1.15	0.89, 1.49		
≥2	103	84	1.47	1.04, 2.09	0.02	1.38	0.96, 1.98	0.08	
Relation of smoking relative(s) in adulthood									
Spouse	365	320	1.38	1.08, 1.76		1.31	1.01, 1.70	1.32	1.03, 1.71
Parent	122	120	1.18	0.86, 1.63		1.15	0.82, 1.60		
Sibling	27	24	1.26	0.70, 2.27		1.22	0.67, 2.25	0.94	0.67, 1.33
Child	29	30	1.37	0.76, 2.45		1.27	0.69, 2.33		
Other	28	29	1.07	0.60, 1.91		0.98	0.53, 1.83		
Passive smoking at workplace									
No	424	438	1.00	Referent		1.00	Referent		
Yes	236	231	1.04	0.82, 1.31		1.00	0.79, 1.27		

^a Adjusted for age and geographic area.

^b Adjusted for age, geographic area, education level, current housing type, current occupation, first-degree family history of nasopharyngeal carcinoma, tea drinking, and salt-preserved fish consumption in 2000–2002.

^c Adjusted for age, geographic area, residential passive smoking during childhood, and residential passive smoking from a spouse during adulthood.

^d Those never exposed to residential passive smoking in childhood were the reference group for all comparisons with childhood residential passive smoking exposure.

^e Those never exposed to residential passive smoking in adulthood were the reference group for all comparisons with adulthood residential passive smoking exposure.