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Morbidity and mortality in relation to smoking among women and men of Chinese ethnicity: The Singapore Chinese Health Study

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ABSTRACT

Objectives: We examined the association among cigarette smoking, smoking cessation and a broad range of cancer incidence and all cause and cause-specific mortality in a population-based cohort of adults of Chinese ethnicity in Singapore.

Methods: Subjects were 61,320 participants of the Singapore Chinese Health Study (44.5% men, aged 45–74 years, recruitment from 1993–1998) who were free of cancer at the baseline examination. Main outcomes-of-interest included cancer incidence, all cause and cause-specific mortality as of December 31, 2005.

Results: Cigarette smoking was positively associated with overall cancer incidence, including cancers at the following specific sites: head and neck region, upper gastrointestinal tract, hepatobiliary and pancreas cancer, lung, and bladder/renal pelvis cancer. Compared to never smokers, the relative risk (RR) (95% confidence interval [CI]) of cancer incidence (all cancer sites) among current smokers smoking >22 cigarettes/day was 1.9 (1.7–2.1), p-trend < 0.0001. Similarly, cigarette smoking was associated with all cause and cause-specific mortality, including deaths due to cancer, ischemic heart disease, other heart diseases, and chronic obstructive pulmonary disease. Compared to never smokers, RR (95%CI) of all cause mortality among current smokers smoking >22 cigarettes/day was 1.8 (1.6–2.0), p-trend < 0.0001. Also, relative to current smokers, ex-smokers experienced reduced cancer incidence and total mortality. The population attributable risk of smoking in men for cancer incidence as well as all-cause mortality was 23%, whereas in women it ranged from 4–5%.

Conclusions: Cigarette smoking is an important risk factor for cancer incidence and major causes of mortality in Chinese men and women of Singapore.

1. Introduction

Cigarette smoking is an important public health problem and a major cause of morbidity and mortality.[1] Numerous epidemiologic studies in Western populations have reported a positive association between cigarette smoking and cancer, cardiovascular disease, chronic obstructive pulmonary disease (COPD), total and cause-specific mortality.[2–26] In

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contrast, relatively few prospective studies from Asia, including studies from China[27,28] and East Asian and other countries[29–37] have examined morbidity and mortality in relation to smoking. Most of these reports exclusively studied men[27,30–32,37]; among the few studies that included women,[28,29,33–36], only two included women of Chinese ethnicity.[28,36] While previous Asian studies examined smoking in relation to coronary heart disease (CHD),[29–31] stroke incidence[29,31,33,35] and cause-specific mortality,[27,28,30,32,36], only two prospective studies examined cancer incidence.[27,34] Studies in Western populations have examined the effect of smoking cessation on morbidity and mortality[10–18,26]; in contrast, only one prospective Asian study examined the relationship between smoking cessation and cardiovascular mortality,[33] but not other mortality causes or cancer incidence. In this context, we examined the association among cigarette smoking, smoking cessation and a broad range of cancer incidence and all cause and cause-specific mortality in a population-based cohort of adult Singaporeans of Chinese ethnicity, the Singapore Chinese Health Study.

2. Patients and methods

2.1. Study population

The design of the Singapore Chinese Health Study has been described previously.[38] Briefly, the cohort was recruited between 1993 and 1998, drawn from permanent residents or citizens of Singapore who lived in government-built housing (86% of the Singapore population resided in such facilities during enrollment period). Men and women of Chinese ethnicity (restricting to the two major dialect groups, the Cantonese and the Hokkiens), aged 45–74 years, were eligible. A total of 63,257 persons (~85% of eligible subjects) were enrolled. At recruitment, a face-to-face interview was conducted in the subject's home by a trained interviewer using a structured, scanner-readable questionnaire, which requested information on demographics, educational attainment, lifetime use of tobacco, current use of alcohol, current level of physical activity, medical history and family history of cancer. The questionnaire included a validated, semi-quantitative food frequency section listing 165 food items commonly consumed in the study population. The Singapore Food Composition Table,[38] which we developed in conjunction with this cohort study, allowed for the estimation of intake levels of approximately 100 nutritive/non-nutritive food components per study subject.

2.2. Exposure assessment

The study population was divided into never, former, and current smokers based on their choice of three possible responses to the following question, 'Have you ever smoked at least 1 cigarette a day for 1 y or longer?' Subjects who answered 'no' were classified as 'non smokers,' those who answered 'yes, but I quit smoking' were classified as 'former smokers,' and those answered 'yes, and I currently smoke' were classified as 'current smokers.' There were six predefined categories of average number of cigarettes smoked/day: ⩽6 cigarettes, 7–12 cigarettes, 13–22 cigarettes, 23–32 cigarettes, 33–42 cigarettes, and ⩾43 cigarettes. The number of years since quitting smoking for former smokers was categorised as: <1 year, 1–2 years, 3–4 years, 5–9 years, 10–14 years, 15–19 years, and ⩾20 years. For the current analysis, based on sample size considerations, we categorised cigarette smoking status into four categories: non smoker, former smoker, current smoker with ⩽22 cigarettes/ day, current smoker with >22 cigarettes/ day. Also, for former smokers, the number of years since quitting smoking was categorised as follows: <10 years, and 10 or more years.

Age was defined as the age in years at the time of baseline examination; education was categorised into no formal education, primary school, secondary school or above; alcohol intake was assessed as grams of daily ethanol consumption; body mass index (BMI) was calculated as weight (kilograms) divided by the square of height (metres); moderate physical activities included brisk walking, bowling, cycling on level ground, tai chi, or chi kung, and hours/week spent on such activities were categorised into none, 1/2 to 3 h/week, ⩾4 h/week.

2.3. Cancer incidence and cause-specific mortality

We identified cancer cases through the population-based Singapore Cancer Registry which has been continuously included in the International Agency for Research on Cancer (IARC) serial publications on world-wide cancer incidence since 1968.[39] Deaths were identified through record linkage with the Singapore Registry of Births and Deaths. In our recent follow-up telephone/in-person interview conducted between 1999 and 2004, among the 61,685 subjects (97.5%) that we had contact or follow-up information, either from themselves, their next-of-kin or death records, only 17 subjects (0.03%) have migrated out of Singapore. This suggests that emigration is negligible among the subjects in the cohort.

Of the 63,257 cohort participants, 1937 had a history of invasive cancer (except for nonmelanoma skin cancer) or *in situ* bladder cancer at recruitment, thus were excluded from the current analysis. As of December 31, 2005, among the 61,320 participants who were free of cancer at baseline, a total of 7982 had died and 5253 had developed either incident invasive cancer of any site or *in-situ* cancer of the bladder and cervix (for females only). Among the cancer cases, 4750 cases (90.4%) had histopathological diagnoses while the remaining 503 cases (9.6%) were diagnosed using clinical or radiological evidence. In addition, histological information on 4407 cancer diagnoses (83.9%) were verified via manual review of all pathology reports and 218 cases (4.2%) were verified via review of medical records by medically trained research staff.

2.4. Statistical analysis

Person-years for each cohort participant was counted from the date of interview to date of cancer diagnosis (for cancer morbidity analysis), or date of death, or December 31 2005, whichever occurred first. We examined two smoking-related exposures, assessed at the baseline examination: (1) categories of smoking status (non smoker [referent category], former smoker, current smoker with ⩽22 cigarettes/ day,

current smoker with >22 cigarettes/day), and (2) categories related to smoking cessation (current smoker [referent category], <10 years since quitting, ⩾10 years since quitting, never smoker). We were interested in two groups of outcomes: (1) cancer at all sites and site-specific cancer incidence (based on first diagnosed primary site of cancer categorised according to International Classification of Diseases, Tenth Revision [ICD-10] code), and (2) all cause and cause-specific mortality (based on underlying cause of death classification according to International Classification of Diseases, Ninth Revision [ICD-9] code from death certificates). The following cancer sites (ICD-10 code) were studied: all cancer sites (C00-C97), head and neck (C00.0-C14.8, C32.0-C32.9), upper gastrointestinal tract (oesophagus [C15.2-C15.9] and stomach [C16.0-C16.9]), colorectal cancer (colon [C18.0-C18.9] and rectum [C19]), hepatobiliary and pancreas cancer (liver and intrahepatic bile ducts[C22], gallbladder and other biliary tract [C23, 24] and pancreas [C25.0-C25.9]), lung (C34.0-C34.9), bladder and renal pelvis cancer (C65.0-C68.9), and breast cancer (women only) (C50). We counted only invasive cancers in defining incident cancer, except for bladder cancer (C67) and cervical cancer (C53), where *in situ* cancers were also included in the analysis. In the current analysis, we were interested in the global association between smoking and a broadly defined range of site-specific incident cancers. We initially performed separate analyses for liver (C22), pancreas (C25) and gallbladder/ other biliary tract (C23, 24) cancers. Since these sites showed similar positive association with smoking, we combined these categories into a single group, 'hepatobiliary and pancreas cancer', to obtain adequate sample size. Similarly, after separate analyses that showed similar associations, we chose to combine bladder (C67), and renal pelvis and other urinary organs (C65, C66, C68) into a single group, 'bladder/renal pelvis cancer'. Breast cancer analyses are confined to women. There were very few bladder/renal pelvis cancer among women smokers (35 cases). Therefore, we presented results of both men and women combined. Mortality due to the following specific causes (ICD-9 code) were studied: cancer (140–208), ischemic heart disease (410–414), stroke (430–438), other heart diseases (391–398, 401, 402, 404, 415–417, 420–429), chronic obstructive pulmonary disease (COPD) (490–496), and liver cirrhosis (571). We used multivariable-adjusted proportional hazards models to estimate the relative risk (RR) and 95% confidence intervals (CI), controlling simultaneously for potential confounders, including age (years), gender (males, females), dialect group (Cantonese, Hokkien), year of recruitment, level of education (no formal education, primary school, secondary school or above), daily ethanol intake (grams), and h/week of moderate physical activity (none, 1/2 to 3 h/week, 4 h/week or more). Additional variables considered as potential confounders but not included in the final multivariable model were as follows: total calorie intake (kcal/day), total fruits (g/day), total vegetables (g/day), total red meats (g/day), dietary fibre (g/day), dietary cholesterol (mg/day), vitamin E (mg/day), weekly vitamin supplement use (yes, no), and among women, menopausal status (premenopausal, postmenopausal), and post-menopausal oestrogen use (current, former, never). We analysed cigarette smoking categories as an ordinal variable in multivariable models to examine trend in the association. We used cross-product interaction terms in regression models to test multiplicative interaction. We calculated the population attributable risk in relation to ever smoking using Levin's formula.[40] All analyses were conducted using SAS version 9.2 (SAS Inc; Cary, NC). Statistical significance was defined as 2-sided p-value < 0.05.

3. Results

Table 1 presents the baseline characteristics of the cohort by smoking status. Approximately 20% of all cohort participants

Table 1 – Selected baseline characteristics by smoking status[a]

	Men (n = 27,292)			Women (n = 34,028)		
	Never smoker	Former smoker	Current smoker	Never smoker	Former smoker	Current smoker
No. of subjects	11,521 (42.2%)	5838 (21.4%)	9933 (36.4%)	31,062 (91.3%)	842 (2.5%)	2124 (6.2%)
Mean age, years	55.3	59.0	56.7	55.7	63.1	60.8
Highest education						
No formal education	859 (29.0%)	602 (20.3%)	1500 (50.7%)	11881 (86.7%)	471 (3.4%)	1348 (9.8%)
Primary school	4964 (35.6%)	3294 (23.6%)	5682 (40.8%)	12324 (92.8%)	301 (2.3%)	658 (5.0%)
Secondary school or above	5698 (54.8%)	1942 (18.7%)	2751 (26.5%)	6857 (97.3%)	70 (1.0%)	118 (1.7%)
Alcohol intake frequency						
Never	8385 (44.8%)	4151 (22.2%)	6175 (33.0%)	28362 (91.7%)	741 (2.4%)	1835 (5.9%)
Monthly	1293 (44.3%)	584 (20.0%)	1040 (35.7%)	1409 (89.4%)	50 (3.2%)	118 (7.5%)
Weekly	1472 (37.8%)	782 (20.1%)	1643 (42.2%)	991 (88.4%)	34 (3.0%)	96 (8.6%)
Daily	371 (21.0%)	321 (18.2%)	1075 (60.8%)	300 (76.5%)	17 (4.3%)	75 (19.1%)
Mean daily ethanol intake, g	2.0	3.1	5.8	0.3	0.6	0.9
Mean body mass index, kg/m^2	23.3	23.3	22.5	23.3	23.4	22.7
Hours/week of moderate physical activity						
No	8282 (40.2%)	4201 (20.4%)	8098 (39.4%)	24694 (90.8%)	660 (2.4%)	1858 (6.8%)
1/2 to 3 h/week	2080 (49.6%)	981 (23.4%)	1133 (27.0%)	4029 (93.3%)	121 (2.8%)	168 (3.9%)
4 h/week or more	1159 (46.1%)	656 (26.1%)	702 (27.9%)	2339 (93.6%)	61 (2.4%)	98 (3.9%)

a Row percentages in parentheses are presented together with number of subjects in each cell, unless otherwise stated.

(36% of men and 6% of women) reported smoking cigarettes at recruitment. Current smokers had lower levels of education and BMI, higher mean intake of alcohol, and were physically less active.

Table 2 presents the relation between categories of smoking status at baseline and cancer incidence. We observed a positive association between increasing smoking levels and risks of total cancer as well as cancer of the head and neck,

Table 2 – Relation between smoking categories and cancer incidence

Cancer sites	Never smoker	Former smoker	Current smoker		p-trend
			⩽22 cigarettes/day	>22 cigarettes/day	
All cancers					
No. of cases, whole cohort (*n* = 5253)	2965	711	1272	305	
No. of cases, men (*n* = 2741)	801	621	1034	285	
No. of cases, women (*n* = 2512)	2164	90	238	20	
Multivariable RR[a], whole cohort	1 (Referent)	1.2 (1.1–1.3)	1.60 (1.5–1.7)	1.9 (1.7–2.1)	<0.0001
Multivariable RR[a], men	1 (Referent)	1.2 (1.1–1.4)	1.70 (1.6–1.9)	1.9 (1.7–2.2)	<0.0001
Multivariable RR[a], women	1 (Referent)	1.3 (1.0–1.6)	1.45 (1.3–1.7)	2.1 (1.4–3.3)	<0.0001
Head and neck cancer					
No. of cases, whole cohort (*n* = 345)	149	48	114	34	
No. of cases, men (*n* = 252)	72	45	104	31	
No. of cases, women (*n* = 93)	77	3	10	3	
Multivariable RR[a], whole cohort	1 (Referent)	1.2 (0.85–1.7)	2.1 (1.6–2.71)	2.5 (1.6–3.7)	<0.0001
Multivariable RR[a], men	1 (Referent)	1.1 (0.78–1.7)	2.0 (1.5–2.76)	2.3 (1.5–3.5)	<0.0001
Multivariable RR[a], women	1 (Referent)	1.7 (0.54–5.6)	2.1 (1.1–4.12)	9.9 (3.1–32.0)	0.0005
Upper gastrointestinal tract cancer					
No. of cases, whole cohort (*n* = 458)	222	75	127	34	
No. of cases, men (*n* = 294)	83	67	112	32	
No. of cases, women (*n* = 164)	139	8	15	2	
Multivariable RR[a], whole cohort	1 (Referent)	1.2 (0.88–1.6)	1.5 (1.2–1.9)	1.7 (1.2–2.5)	0.0004
Multivariable RR[a], men	1 (Referent)	1.1 (0.82–1.6)	1.6 (1.2–2.1)	1.8 (1.2–2.7)	0.0003
Multivariable RR[a], women	1 (Referent)	1.6 (0.78–3.3)	1.1 (0.66–1.9)	2.7 (0.67–11.01)	0.26
Colorectal cancer					
No. of cases, whole cohort (*n* = 931)	550	150	201	30	
No. of cases, men (*n* = 514)	185	138	162	29	
No. of cases, women (*n* = 417)	365	12	39	1	
Multivariable RR[a], whole cohort	1 (Referent)	1.1 (0.92–1.4)	1.2 (0.97–1.4)	0.83 (0.56–1.2)	0.46
Multivariable RR[a], men	1 (Referent)	1.2 (0.95–1.5)	1.2 (0.96–1.5)	0.87 (0.58–1.3)	0.47
Multivariable RR[a], women	1 (Referent)	0.82 (0.46–1.5)	1.2 (0.84–1.7)	0.54 (0.08–3.9)	0.61
Hepatobiliary and pancreas cancer					
No. of cases, whole cohort (*n* = 480)	235	80	136	29	
No. of cases, men (*n* = 322)	107	72	115	28	
No. of cases, women (*n* = 158)	128	8	21	1	
Multivariable RR[a], whole cohort	1 (Referent)	1.1 (0.85–1.5)	1.5 (1.2–1.9)	1.4 (0.92–2.1)	0.002
Multivariable RR[a], men	1 (Referent)	1.1 (0.77–1.4)	1.4 (1.1–1.8)	1.3 (0.86–2.0)	0.02
Multivariable RR[a], women	1 (Referent)	1.6 (0.79–3.4)	1.8 (1.1–2.9)	1.6 (0.22–11.5)	0.009
Lung cancer					
No. of cases, whole cohort (*n* = 905)	254	132	391	128	
No. of cases, men (*n* = 628)	77	110	321	120	
No. of cases, women (*n* = 277)	177	22	70	8	
Multivariable RR[a], whole cohort	1 (Referent)	2.1 (1.6–2.6)	4.8 (4.0–5.7)	7.9 (6.2–10.0)	<0.0001
Multivariable RR[a], men	1 (Referent)	2.0 (1.5–2.7)	5.0 (3.9–6.4)	7.9 (5.9–10.6)	<0.0001
Multivariable RR[a], women	1 (Referent)	2.7 (1.7–4.3)	4.3 (3.2–5.7)	8.3 (4.0–17.1)	<0.0001
Bladder/renal pelvis cancer					
No. of cases, whole cohort (*n* = 146)	61	33	40	12	
Multivariable RR[a], whole cohort	1 (Referent)	1.5 (0.96–2.5)	1.7 (1.1–2.7)	2.7 (1.4–5.2)	0.002
Breast cancer (women only)					
No. of cases, women (*n* = 534)	491	14	28	1	
Multivariable RR[a], women	1 (Referent)	1.2 (0.68–2.0)	0.97 (0.66–1.4)	0.58 (0.08–4.1)	0.87

a Relative risk (95% confidence interval) estimated from a multivariable-adjusted proportional hazards model adjusted for age (years), gender (males, females), dialect group (Cantonese, Hokkien), year of recruitment, level of education (no formal education, primary school, secondary school or above), daily ethanol intake (g), and h/week of moderate physical activity (none, 1/2 to 3 h/week, 4 h/week or more).

upper gastrointestinal tract, hepatobiliary and pancreas, lung, and bladder/renal pelvis. Smoking was unrelated to the overall risk of colorectal cancer. A null association between smoking and breast cancer risk was noted in this study population. In a subsidiary analysis, women who began to smoke before 15 years of age had a relative risk of 1.7 (95% CI = 0.97–3.1) compared with never smokers.

In Table 3, we observed a positive association between increasing smoking categories and all cause mortality and the following cause-specific deaths: cancer, ischemic heart disease, and COPD. We also observed a positive association between smoking and other heart disease mortality, the RR estimates were similar to the results for ischemic heart disease (data not shown). A positive association between smoking and mortality due to liver cirrhosis was of borderline statistical significance (data not shown). Compared to never smokers (referent group), the RR (95% CI) of liver cirrhosis mortality ($n = 78$) was 1.2 (0.60–2.4) among former smokers, 1.3 (0.70–2.5) among current smokers smoking ⩽22cigarettes/day, and 2.0 (0.85–4.7) among current smokers smoking >22 cigarettes/day, p-trend = 0.06. There was no overall association between smoking and stroke mortality.

Table 4 presents the effect of smoking cessation on cancer incidence. For all cancers, we observed a statistically significant risk reduction for former smokers, and the risk reduction was dependent on the number of years of smoking cessation. Compared to current smokers, the RR (95% CI) for all cancers was 0.84 (0.75–0.94) for former smokers with <10 years and 0.67 (0.59–0.75) for former smokers with at least 10 years since smoking cessation. Similarly, a statistically significant, inverse associations was observed between the number of years since smoking cessation and the risk of developing cancer of the head and neck, upper gastrointestinal tract, hepatobiliary and pancreas, lung, and bladder/renal pelvis (Table 4).

Table 3 – Relation between smoking categories and mortality

Cause of death	Never smoker	Former smoker	Current smoker		p-trend
			⩽22 cigarettes/day	>22 cigarettes/day	
All causes					
No. of deaths, whole cohort ($n = 7982$)	3945	1340	2228	469	
No. of deaths, men ($n = 4706$)	1325	1146	1802	433	
No. of deaths, women ($n = 3276$)	2620	194	426	36	
Multivariable RR[a], whole cohort	1 (Referent)	1.3 (1.2–1.4)	1.7 (1.6–1.8)	1.8 (1.6–2.0)	<0.0001
Multivariable RR[a], men	1 (Referent)	1.3 (1.2–1.4)	1.7 (1.6–1.8)	1.7 (1.5–1.9)	<0.0001
Multivariable RR[a], women	1 (Referent)	1.7 (1.4–1.9)	1.6 (1.4–1.8)	2.5 (1.8–3.5)	<0.0001
Cancer					
No. of deaths, whole cohort ($n = 2710$)	1271	402	835	202	
No. of deaths, men ($n = 1618$)	403	344	685	186	
No. of deaths, women ($n = 1092$)	868	58	150	16	
Multivariable RR[a], whole cohort	1 (Referent)	1.3 (1.2–1.5)	2.1 (1.9–2.3)	2.4 (2.0–2.8)	<0.0001
Multivariable RR[a], men	1 (Referent)	1.3 (1.1–1.4)	2.1 (1.9–2.4)	2.3 (2.0–2.8)	<0.0001
Multivariable RR[a], women	1 (Referent)	1.7 (1.3–2.3)	1.9 (1.6–2.3)	3.6 (2.2–5.9)	<0.0001
Ischemic heart disease					
No. of deaths, whole cohort ($n = 1664$)	799	300	479	86	
No. of deaths, men ($n = 1030$)	291	258	402	79	
No. of deaths, women ($n = 634$)	508	42	77	7	
Multivariable RR[a], whole cohort	1 (Referent)	1.3 (1.2–1.5)	1.7 (1.5–1.9)	1.6 (1.3–2.0)	<0.0001
Multivariable RR[a], men	1 (Referent)	1.3 (1.1–1.6)	1.8 (1.5–2.1)	1.6 (1.2–2.0)	<0.0001
Multivariable RR[a], women	1 (Referent)	1.7 (1.2–2.3)	1.4 (1.1–1.8)	2.4 (1.1–5.1)	0.0002
Stroke					
No. of deaths, whole cohort ($n = 832$)	476	136	193	27	
No. of deaths, men ($n = 436$)	149	119	145	23	
No. of deaths, women ($n = 396$)	327	17	48	4	
Multivariable RR[a], whole cohort	1 (Referent)	1.1 (0.89–1.4)	1.2 (1.0–1.4)	0.86 (0.57–1.3)	0.27
Multivariable RR[a], men	1 (Referent)	1.1 (0.85–1.4)	1.1 (0.89–1.4)	0.74 (0.47–1.2)	0.93
Multivariable RR[a], women	1 (Referent)	1.0 (0.62–1.7)	1.3 (0.98–1.8)	2.1 (0.80–5.8)	0.03
Chronic obstructive pulmonary disease					
No. of deaths, whole cohort ($n = 378$)	85	97	162	34	
No. of deaths, men ($n = 282$)	36	87	126	33	
No. of deaths, women ($n = 96$)	49	10	36	1	
Multivariable RR[a], whole cohort	1 (Referent)	3.6 (2.6–5.0)	4.9 (3.7–6.5)	5.6 (3.6–8.6)	<0.0001
Multivariable RR[a], men	1 (Referent)	3.1 (2.1–4.6)	4.1 (2.8–5.9)	5.0 (3.1–8.0)	<0.0001
Multivariable RR[a], women	1 (Referent)	4.0 (2.0–8.1)	6.6 (4.3–10.2)	3.5 (0.49–25.6)	<0.0001

a Relative risk (95% confidence interval) estimated from a multivariable-adjusted proportional hazards model adjusted for age (years), gender (males, females), dialect group (Cantonese, Hokkien), year of recruitment, level of education (no formal education, primary school, secondary school or above), daily ethanol intake (g), and h/week of moderate physical activity (none, 1/2 to 3 h/week, 4 h/week or more).

Table 4 – Relation between smoking cessation and cancer incidence

Cancer site	Current smoker	Years since quitting among former smokers		Never smoker
		<10 years	⩾10 years	
All cancers				
No. of cases, whole cohort (n = 5253)	1577	356	355	2965
Multivariable RR[a], whole cohort	1 (Referent)	0.84 (0.75–0.94)	0.67 (0.59–0.75)	0.61 (0.57–0.66)
Head and neck cancer				
No. of cases, whole cohort (n = 345)	148	31	17	149
Multivariable RR[a], whole cohort	1 (Referent)	0.81 (0.55–1.2)	0.37 (0.22–0.61)	0.47 (0.36–0.61)
Upper gastrointestinal tract cancer				
No. of cases, whole cohort (n = 458)	161	38	37	222
Multivariable RR[a], whole cohort	1 (Referent)	0.87 (0.61–1.3)	0.69 (0.48–1.0)	0.66 (0.52–0.84)
Hepatobiliary and pancreas cancer				
No. of cases, whole cohort (n = 480)	165	31	49	235
Multivariable RR[a], whole cohort	1 (Referent)	0.67 (0.46–0.99)	0.85 (0.62–1.2)	0.69 (0.54–0.86)
Lung cancer				
No. of cases, whole cohort (n = 905)	519	88	44	254
Multivariable RR[a], whole cohort	1 (Referent)	0.59 (0.47–0.74)	0.23 (0.17–0.32)	0.20 (0.16–0.23)
Bladder/renal pelvis cancer				
No. of cases, whole cohort (n = 146)	52	21	12	61
Multivariable RR[a], whole cohort	1 (Referent)	1.2 (0.75–2.1)	0.52 (0.27–0.98)	0.54 (0.36–0.82)

a Relative risk (95% confidence interval) estimated from a multivariable-adjusted proportional hazards model adjusted for age (years), gender (males, females), dialect group (Cantonese, Hokkien), year of recruitment, level of education (no formal education, primary school, secondary school or above), daily ethanol intake (g), and h/week of moderate physical activity (none, 1/2 to 3 h/week, 4 h/week or more).

Table 5 – Relation between smoking cessation and mortality

Cause of death	Years since quitting among former smokers			Never smoker
	Current smoker	<10 years	⩾10 years	
All causes				
No. of deaths, whole cohort (n = 7982)	2697	702	638	3945
Multivariable RR[a], whole cohort	1 (Referent)	0.91 (0.84–0.99)	0.65 (0.60–0.71)	0.59 (0.55–0.62)
Cancer				
No. of deaths, whole cohort (n = 2710)	1037	222	180	1271
Multivariable RR[a], whole cohort	1 (Referent)	0.77 (0.67–0.89)	0.50 (0.42–0.58)	0.47 (0.43–0.52)
Ischemic heart disease				
No. of deaths, whole cohort (n = 1664)	565	159	141	799
Multivariable RR[a], whole cohort	1 (Referent)	0.96 (0.80–1.1)	0.66 (0.55–0.80)	0.60 (0.53–0.67)
Chronic obstructive pulmonary disease				
No. of deaths, whole cohort (n = 378)	196	59	38	85
Multivariable RR[a], whole cohort	1 (Referent)	1.0 (0.75–1.3)	0.50 (0.35–0.71)	0.20 (0.15–0.27)

a Relative risk (95% confidence interval) estimated from a multivariable-adjusted proportional hazards model adjusted for age (years), gender (males, females), dialect group (Cantonese, Hokkien), year of recruitment, level of education (no formal education, primary school, secondary school or above), daily ethanol intake (g), and h/week of moderate physical activity (none, 1/2 to 3 h/week, 4 h/week or more).

Table 5 presents the effect of smoking cessation on all cause and selected cause-specific mortality. A statistically significant reduction in risk of all-cause mortality and cause-specific mortality was noted among former smokers. Compared with current smokers, the RR (95% CI) for all-cause mortality was 0.91 (0.84–0.99) for former smokers with <10 years since smoking cessation and 0.65 (0.60–0.71) for those who quit smoking at least 10 years.

Table 6 presents the population attributable risk of cancer incidence and cause-specific mortality in relation to ever smoking. Smoking accounted for more than one in five cancer cases as well as all-cause deaths in men whereas about 4–5% of cancer and death burdens were attributable to smoking in women.

4. Discussion

In a large population-based cohort of adult Chinese Singaporeans, cigarette smoking was positively associated with risk of developing any cancer as well as certain specific cancer

Table 6 – Population attributable risk (PAR) of cancer morbidity and all cause and cause-specific mortality to cigarette smoking

	Relative risk (95% confidence interval) associated with ever smoking[a]		Population attributable risk associated with ever smoking	
	Men	Women	Men	Women
Cancer morbidity				
All cancers	1.5 (1.4–1.7)	1.4 (1.3–1.6)	23.0%	3.6%
Head and neck cancer	1.7 (1.3–2.3)	2.4 (1.3–4.1)	29.0%	10.5%
Upper gastrointestinal tract cancer	1.4 (1.1–1.9)	1.3 (0.85–2.0)	19.8%	2.7%
Hepatobiliary and pancreatic cancer	1.2 (0.97–1.6)	1.7 (1.2–2.6)	11.9%	6.1%
Lung cancer	4.1 (3.2–5.2)	4.0 (3.1–5.1)	63.8%	20.5%
Bladder/renal pelvis cancer	1.8 (1.2–2.8)	1.3 (0.48–3.3)	32.5%	2.2%
Mortality				
All causes	1.5 (1.4–1.6)	1.7 (1.5–1.8)	22.6%	5.3%
Cancer	1.8 (1.6–2.0)	1.9 (1.7–2.2)	30.8%	7.4%
Ischemic heart disease	1.6 (1.4–1.8)	1.5 (1.2–1.8)	24.3%	4.3%
Chronic obstructive pulmonary disease	3.8 (2.6–5.3)	5.7 (3.8–8.6)	61.3%	29.2%

a Relative risk (95% confidence interval) estimated from a multivariable-adjusted proportional hazards model adjusted for age (years), dialect group (Cantonese, Hokkien), year of recruitment, level of education (no formal education, primary school, secondary school or above), daily ethanol intake (g), and h/week of moderate physical activity (none, 1/2 to 3 h/week, 4 h/week or more).

sites including head and neck, upper gastrointestinal tract, hepatobiliary and pancreas, lung, and bladder/renal pelvis. Similarly, cigarette smoking also was associated with all-cause and cause-specific mortality including deaths due to cancer, ischemic heart disease, other heart diseases, and COPD. Smoking cessation was associated with statistically significant reduction in risk of smoking-related cancers and smoking related causes of death. Overall, smoking accounted for one in four cancer cases and deaths in men and <5% of cancer and death burdens in women of the study population.

Prevalence of smoking was historically extremely low among Asian women,[41–43] and most previous Asian studies examining smoking included only men.[27,30–32,37] The well documented increase in prevalence of cigarette smoking in women in the newly industrialised Asian countries,[44] including Singapore, is postulated to be related, at least in part, to the westernisation[45,46] in lifestyles of those Asian populations. While smoking prevalence has declined in many western developed countries, it remains high among men in newly industrialised Asian countries and its prevalence is increasing among women.[44] Smoking related lung cancer is the third most frequent cancer among women in Singapore.[47] While the age-standardised incidence rate of lung cancer in men has fallen from 60 per 100,000 person-years in 1980 to 45 per 100,000 person-years in 2002, it has remained stable in women at approximately 16 per 100,000 person-years over the last two decades.[47] Our data highlights the potential enormous impact of smoking on population health of this continent.

Our results of an overall positive association between cancer incidence and smoking is consistent with previous prospective studies from Asia[27,34] and agrees with recent reports from the US Surgeon General[1,48] and the International Agency for Research on Cancer[44] on the health impact of smoking.

In the current study, cigarette smoking was unrelated to colorectal cancer overall. In a concurrent, separate report, we described in further details the relationship between cigarette smoking and colorectal cancer by smoking intensity and duration, stratified by sub-site and stage of the disease. We noted that smoking was associated with a statistically significant, 50% increase in risk of rectal cancer, but was unrelated to risk of colon cancer (Tsong et al., submitted). Some[34,49–51] but not all[52–54] prior studies have reported a lack of association between smoking and colorectal cancer. Other studies have examined cofactors such as subject's metabolic genotype in tobacco carcinogen metabolism[55,56] and tumour characteristics[55,57] and found smoking to be associated with subgroups defined by these cofactors.

We noted no overall association between cigarette smoking and breast cancer in Singapore Chinese women. However, there was a hint that women who began smoking at a young age (⩽14 years) might be at risk of breast cancer. This observation is consistent with a recent report that smoking initiation at younger age (adolescence and early adulthood) is associated with increased risk of breast cancer, but that smoking was not associated with breast cancer after first child birth.[58] Most studies,[59–68] including a pooled analysis of 53 epidemiologic studies,[68] reported no association between smoking and female breast cancer although some prior studies have noted a positive association.[69–73] Recent reports from the US Surgeon General[1,48] and the International Agency for Research on Cancer[44] concluded that there is no evidence of an association between smoking and breast cancer among women.[1,44,48]

Our findings of an overall positive association between smoking and all cause and cause-specific mortality other than stroke are consistent with previous studies from Asia[27,74] and the US Surgeon General's report.[1] In the present study, current smoking was not associated with stroke mortality, a finding consistent with many,[29,32,75,76] but not all,[27,31,33,37,77,78] previous studies from Asia. Our findings on stroke mortality are contrary to the US Surgeon General's report[1] which concluded that smoking is positively related to

stroke risk, particularly ischemic stroke and subarachnoid haemorrhage. The US report was predominantly based on studies from Western populations[2,18–26]; only two studies from Asian populations were included.[31,78] One explanation for the observed lack of association may be the reported heterogeneous nature of the association between smoking and stroke subtypes, including a potential lack of association with intracerebral haemorrhage[79] and embolic brain infarction.[80]

The main strengths of the current study include its large sample size, good representation of women, its population-based and prospective follow-up nature, and the high percentage of cancer cases that were diagnosed histopathologically. The nationwide cancer registry has been in place since 1968 and has been shown to be comprehensive in its recording of cancer cases.[81] Thus, cancer case ascertainment can be assumed to be complete. However, although women represent 55% of this cohort, only 8.7% ($n = 2965$) were ever smokers and most women were light smokers (i.e. under one pack/day). The relatively small number of cancer death cases in women smokers prevented an in-depth analysis of smoking in this gender subgroup. Despite these limitations, our data suggest that female smokers were equally at risk for cancer and other major causes of death from chronic diseases as men.

In conclusion, in a large population-based cohort of Chinese men and women in Singapore, cigarette smoking was positively associated with cancer incidence in multiple sites, and with all cause and cause-specific mortality. Smoking cessation, as opposed to continuation of smoking, was associated with reduction in cancer incidence and all cause and cause-specific mortality.

Conflict of interest statement

None declared.

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