Early Health Effects of the Emerging Tobacco Epidemic in China

A 16-Year Prospective Study

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Context.—In recent decades, there has been a rapid and substantial increase in tobacco consumption in China, particularly by men, but little is known from local epidemiologic studies about the pattern of smoking-related deaths.

Objective.—To assess the current health effects of cigarette smoking in Shanghai, China.

Design.—Prospective observational study of mortality in relation to cigarette smoking.

Setting.—Eleven factories in urban Shanghai.

Subjects.—A total of 9351 adults (6494 men and 2857 women) aged 35 to 64 years at baseline survey during the 1970s.

Outcome Measures.—All-cause and cause-specific mortality.

Results.—During an average follow-up of 16 years, 881 men and 207 women died. Among men, 61% had described themselves as current cigarette smokers at baseline, and their overall mortality was significantly greater than that of nonsmokers (relative risk [RR], 1.4; 95% confidence interval [CI], 1.2-1.7; $P<.001$). The excess was almost twice as great (RR, 1.8; 95% CI, 1.5-22; $P<.001$) among the men who had begun smoking before the age of 25 years and was significantly associated with the number of cigarettes smoked ($P<.001$ for trend) after adjustment for other major risk factors. The chief sources of the excess were lung cancer (RR, 3.8; 95% CI, 2.1-6.8; $P<.001$), esophageal cancer (RR, 3.6; 95% CI, 1.2-10.5; $P=.02$), liver cancer (RR, 2.0; 95% CI, 1.1-3.7; $P=.03$), coronary heart disease (RR, 1.8; 95% CI, 1.0-3.2; $P=.04$), and chronic obstructive pulmonary disease (RR, 2.5; 95% CI, 1.4-4.4; $P<.01$). Among the men in this Chinese population, about 20% (95% CI, 12%-29%) of all deaths during the study period could be attributed to cigarette smoking. Of these deaths, one third involved lung cancer, one third involved other cancers, and one third involved other diseases. Only 7% of women described themselves as current cigarette smokers at baseline, but among them there was also a statistically significant excess of overall mortality (RR, 1.7; 95% CI, 1.2-2.5; $P<.01$).

Conclusions.—Cigarette smoking is already a major cause of death in China, and among middle-aged Shanghai men, about 20% of all deaths during the 1980s were due to smoking. The excess was greatest among men who began smoking before the age of 25 years, about 47% of whom would, at 1987 mortality rates, die between the ages of 35 and 69 years (compared with only 29% of nonsmokers). These estimates reflect the consequences of past smoking patterns. The future health effects of current smoking patterns are likely to be greater because of the recent large increase in cigarette consumption, particularly at younger ages, in China.

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IN COUNTRIES such as the United States and the United Kingdom where cigarettes have been used widely for several decades, tobacco is now responsible for about one third of all deaths in middle age, with substantial effects on mortality from lung cancer, coronary heart disease (CHD), and chronic obstructive pulmonary disease (COPD).[1-5] In recent decades there has been a rapid and substantial increase in tobacco consumption in China, particularly by men.[6,7]

See also pp 1505 and 1531.

Based on Western experience, it has been estimated that, if current smoking patterns persist, tobacco will eventually cause more than 2 million deaths each year in China.[8,9] But there is little direct epidemiologic evidence about the evolution of this epidemic in China, where, although about two thirds of men are now smokers,[6,7] the main increase in cigarette consumption, especially among younger people, has been too recent for its full effects on health yet to be seen. This report is of a 16-year prospective study of smoking and mortality in Shanghai.

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METHODS

Baseline Survey

The study population consisted of 9351 middle-aged adults from 11 factories (mainly involved in the manufacture of general and electrical machinery and equipment) in urban Shanghai. The baseline survey was conducted in 1972 and 1973 for 3 factories (1635 men and 1288 women) and in 1977 and 1978 for the remaining 8 factories (4859 men and 1569 women).[10,11] Factory employees aged 35 to 64 years were interviewed at screening clinics by trained health workers using a standardized questionnaire, and information was obtained on smoking, alcohol consumption, occupation, medical history, and physical exercise. Height, weight, and blood pressure were also recorded. Blood was taken for measurement of serum cholesterol, and a resting electrocardiogram was performed. Current cigarette smokers were defined as those who reported smoking at least 1 cigarette a day during the 6-month period immediately before the interview. No information on other tobacco consumption or on ex-smokers was collected at baseline.

Repeat Survey

A repeat survey was conducted in 7 of the factories about 3 years after the baseline survey. Information on current smoking status was collected in 4355 subjects (80% of those originally surveyed in those factories). Of those classified as nonsmokers at baseline, 95% remained so at resurvey. Among those who smoked 1 to 19 or 20 or more cigarettes daily at baseline, 79% and 90%, respectively, continued to report themselves as current smokers at resurvey.

Follow-up

Vital status was monitored regularly through factory records until January 1, 1993. This yields a mean follow-up duration of 16 years during which 389 individuals (4%) were lost to follow-up and 1088 (12%) died. Causes of death were sought chiefly from official death certificates, supplemented, if necessary, by hospital records and by inquiry of family members or factory medical staff. The underlying cause of each death was coded by 2 trained nosologists blinded to smoking status in the Shanghai Sanitary and Anti-Epidemic Station using the *International Classification of Diseases, Ninth Revision* (*ICD-9*).

Statistical Analysis

Analyses for men and women were conducted separately. For men, 3 categories of baseline smoking were used: nonsmoker, current smoker of 1 to 19 cigarettes per day, and current smoker of 20 or more cigarettes per day. For women, because of the relatively small number studied and their low smoking prevalence, only 2 categories of baseline smoking were used: nonsmoker and current cigarette smoker. The standardized mortality rate was calculated using the indirect method in a particular smoking category, adjusted for age (by 5-year groups) and factory. The Cox proportional hazards model[12] was also used to estimate relative risks (RRs) and their corresponding 95% confidence intervals (CIs), which compared various categories of cigarette smokers with nonsmokers, adjusting simultaneously for various baseline variables. When there was more than 1 current smoking category, floating variances were used.[13,14] These leave the RR estimates unchanged but, by ascribing some variation to the results for the reference group, provide more appropriate CIs.

RESULTS

Prevalence of Cigarette Smoking at Baseline

At the baseline survey, 61% of men and 7% of women described themselves as current cigarette smokers. Forty-six percent of these male smokers reported consuming 20 or more cigarettes per day, compared with only 11% of the female smokers. Among male smokers, 38% had started smoking before the age of 25 years, and 62% had begun at a later age; the corresponding figures among female smokers were 25% and 75%. Individuals who had started smoking at an early age were particularly likely to be heavy smokers: 56% of men who had started before the age of 25 years consumed 20 or more cigarettes daily compared with 41% of those who had started later; the corresponding figures for women were 24% and 8%.

Causes of Death

By January 1, 1993, 881 deaths had been recorded in men and 207 in women. Of these 433 (40%) were attributed to neoplastic disease (*ICD-9* code 140-239), including 109 from lung cancer, 97 from stomach cancer, 79 from liver cancer, 33 from esophageal cancer, and 33 from intestinal cancer. A further 384 deaths (35%) were attributed to cardiovascular disease (*ICD-9* code 390-459), including 86 (8%) from CHD and 256 (23%) from stroke. Chronic obstructive pulmonary disease (*ICD-9* code 490-496) accounted for 93 deaths (9%). There were 130 deaths (12%) from other known causes and 33 (3%) from unknown causes.

Cancer Mortality by Smoking Habit Among Men

Among men, cigarette smoking was significantly associated with death from cancer (Table 1). The total cancer mortality rates per 100 000 persons were 231 for nonsmokers compared with 364 for those smoking 1 to 19 cigarettes daily and 478 for those smoking 20 or more cigarettes a day ($P<.001$ for trend). Compared with nonsmokers, the overall RR among smokers was 1.8 (95% CI, 1.4-2.3; $P<.001$), suggesting that about one third of all male cancer deaths were due to tobacco.

Most of the excess cancer mortality among male smokers was due to excesses of lung, esophageal, and liver cancer, each of which was separately significant. In comparison with nonsmokers, the RR of lung cancer for smokers was 3.8 ($P<.001$). Hence, about 63% of male lung cancer deaths (95% CI, 52%-78%) during the study period could be attributed to smoking. There was also a strong positive dose-response effect between risk and the number of cigarettes smoked ($P<.001$ for trend). For lung cancer, the relationship between risk and age of starting to smoke was also examined (Table 2). Relative to nonsmokers, the risks of lung cancer were particularly large among men who had started before the age of 25 years (4.3 and 9.2, respectively, for those who smoked 1-19 cigarettes and ≥20 cigarettes daily). The RR of esophageal cancer among smokers was 3.6 ($P=.02$) and of liver cancer was 2.0 ($P=.03$). Only for the former was there a significant trend for higher risk among heavier smokers. The RR for colorectal cancer was also increased, but this association is based on small numbers of deaths and is not statistically significant. No relationship was observed between cigarette smoking and mortality from stomach cancer or from the aggregate of all other neoplastic diseases, but, again, the number of such deaths was small.

Vascular Mortality by Smoking Habit Among Men

No significant association was seen among men between cigarette smoking and death from all vascular causes (RR, 1.1; 95% CI, 0.9-1.4). Of these vascular deaths, only 69 were attributed to CHD, and these were significantly associated with smoking (RR, 1.8; 95% CI, 1.0-3.2; $P=.04$), with a positive dose-response effect between the risk and the number of cigarettes smoked ($P=.04$ for trend). Mortality from stroke was high (23% of total deaths) but had no apparent association with cigarette smoking, even after adjustment for various other factors (RR, 1.0). Cigarette smoking was associated with a 2-fold risk of death from pulmonary heart disease, but there were only 24 such deaths and the association was not statistically significant. (This condition should, however, perhaps be considered with COPD instead of with vascular disease; see below.) Only 16 male

Table 1.—Age-Standardized Annual Mortality Rates and Relative Risks by Smoking Status at Baseline Among Men

Cause of Death (*ICD-9* Code)†	No. of Deaths	Mortality (and Relative Risks*) per 100 000 Persons				z Values for Trend§	P Values
		All Smokers (61 568‡)	Nonsmokers (40 381‡)	No. of Cigarettes Smoked			
				1-19 Cigarettes per d (34 684‡)	≥20 Cigarettes per d (26 884‡)		
Cancer							
Lung (161)	97	128 (3.8)‖	36 (1.0)	105 (2.8)¶	164 (5.4)‖	5.25	<.001
Esophagus (150)	29	38 (3.6)#	11 (1.0)	30 (2.8)	49 (4.6)¶	2.63	.009
Liver (155)	66	78 (2.0)#	42 (1.0)	77 (2.1)#	80 (1.9)	1.84	.07
Colorectal (153, 154)	22	26 (1.8)	14 (1.0)	22 (1.5)	33 (2.6)	1.51	.13
Stomach (151)	86	87 (1.0)	81 (1.0)	88 (1.1)	84 (0.9)	−0.24	.81
Other neoplastic	51	53 (1.1)	46 (1.0)	43 (0.9)	69 (1.4)	0.83	.41
All neoplastic (140-239)	351	408 (1.8)‖	231 (1.0)	364 (1.6)¶	478 (2.1)‖	4.82	<.001
Vascular disease							
Coronary heart disease (410-414)	69	76 (1.8)#	52 (1.0)	74 (1.7)	80 (2.0)#	2.05	.04
Stroke (430-438)	199	192 (1.0)	201 (1.0)	187 (1.0)	200 (1.1)	0.71	.48
Pulmonary heart disease (416)	24	29 (2.0)	14 (1.0)	35 (2.2)	19 (1.5)	0.76	.45
Other vascular	16	7 (0.3)#	31 (1.0)	7 (0.2)#	8 (0.4)	−1.82	.07
All vascular (390-459)	308	305 (1.1)	298 (1.0)	302 (1.1)	309 (1.2)	1.27	.20
Respiratory disease							
Chronic obstructive pulmonary disease (490-496)	82	103 (2.5)¶	40 (1.0)	83 (1.9)#	139 (3.7)‖	3.95	<.001
Other respiratory	12	9 (0.7)	16 (1.0)	6 (0.4)	14 (1.2)	0.09	.93
All respiratory (460-519)	94	113 (2.0)¶	57 (1.0)	89 (1.5)	152 (3.1)‖	3.72	<.001
Other known causes							
Chronic liver disease (571)	29	34 (1.5)	20 (1.0)	30 (1.3)	39 (1.7)	1.07	.28
Trauma (E800-E999)	18	16 (0.6)	21 (1.0)	16 (0.5)	16 (0.5)	−0.83	.41
Other disease	55	57 (1.1)	49 (1.0)	58 (1.1)	54 (1.2)	0.53	.55
All noncancer, nonvascular, non–chronic obstructive pulmonary disease deaths	102	106 (1.1)	90 (1.0)	104 (1.1)	109 (1.2)	0.69	.49
Unknown causes	26	24 (1.1)	28 (1.0)	32 (1.5)	9 (0.4)	−0.60	.55
All causes	881	955 (1.4)‖	702 (1.0)	890 (1.3)¶	1059 (1.6)‖	5.23	<.001

*Relative risks were estimated in a Cox proportional hazards model, stratified for factories and adjusted for age, systolic blood pressure, serum cholesterol, and regular alcohol drinking (yes vs no) at baseline.
†*ICD-9* indicates *International Classification of Diseases, Ninth Edition.*
‡Observed person-years.
§Trend test is for nonsmoker vs smokers of 1 to 19 vs smokers of 20 or more cigarettes daily.
‖$P<.001$ for comparison with nonsmoker category.
¶$P<.01$ for comparison with nonsmoker category.
#$P<.05$ for comparison with nonsmoker category.

deaths were attributed to other vascular diseases, including 5 from rheumatic heart disease (all in nonsmokers) and 1 from congenital heart disease. The risk of death from this group of other vascular diseases was significantly lower among smokers (RR, 0.3; 95% CI, 0.08-0.8; $P=.02$), perhaps because preexisting rheumatic heart disease prevented smoking.

Respiratory and Other Mortality by Smoking Habit Among Men

There was a strong positive association between cigarette smoking and the overall risk of death from respiratory disease among men. Most of these deaths were attributed to COPD, for which the RR of death among smokers was 2.5 (95% CI, 1.4-4.4; $P<.01$). A strong positive dose-response association was also evident between the risk and the number of cigarettes smoked ($P<.001$ for trend). No significant association was seen between cigarette smoking and mortality from the aggregate of all other causes (RR, 1.1), with the slight trend toward an increase in chronic liver disease not statistically significant.

Total Mortality by Smoking Habit Among Men

Overall, there was a highly significantly increased risk of all-cause mortality associated with smoking in men (RR, 1.4; 95% CI, 1.2-1.7; $P<.001$), with a strong positive dose-response relationship between risk and the number of cigarettes smoked ($P<.001$ for trend). If these associations are largely causal, then in this Chinese male population about 20% (95% CI, 12%-29%) of all deaths are due to cigarette smoking, including 63% of the lung cancer deaths. Of all the deaths caused by tobacco, however, only about one third involved lung cancer, one third other cancers, and one third nonneoplastic diseases. Compared with nonsmokers (39% of all men), the RRs for men who started smoking before the age of 25 years (23%) and later (38%) were 1.84 (95% CI, 1.54-2.20) and 1.24 (95% CI, 1.06-1.46), respectively. At 1987 Shanghai death rates,[15] the probability that a 35-year-old man will die by the age of 69 years is 36%, which, taken together with the present study results, suggests that the corresponding probabilities would be 29% for nonsmokers compared with 47% for smokers who began before the age of 25 years and 35% for those who began later.

Mortality by Smoking Habit Among Women

Because of the relatively small number of women studied and their low smoking prevalence, the analyses in women were confined to only 4 major categories of disease (Table 3). No apparent association of neoplastic deaths was observed (RR, 0.9), but there was a nonsignificant 2-fold RR of lung cancer among female smokers (2.3; 95% CI, 0.6-8.9; $P=.22$, data not shown). There were significant increases among smokers in the RRs of death from vascular disease (2.1; 95% CI, 1.2-3.7; $P=.01$) and from respiratory disease (10.7; 95% CI, 3.4-33.2; $P<.001$). Overall, the risk of all-cause mortality was significantly higher among smokers than nonsmokers, with a relative risk of 1.7 (95% CI, 1.2-2.5; $P<.01$). Hence, in this female population with 7% smoking prevalence, about 5% (95% CI, 1%-9%) of the deaths could be attributed to smoking.

COMMENT

The present study shows that cigarette smoking is a major cause of death in Shanghai, particularly among men. About one fifth of all deaths in middle-aged men can now be attributed to tobacco, with the chief sources of the excess being deaths from lung cancer, esophageal cancer, CHD, and COPD. While far fewer women than men were smokers, there was also a statistically significant excess of overall mortality among women smokers. These results are consistent with recent reports from a less prolonged prospective study of smoking and mortality among 18 000 middle-aged Shanghai men.[16] In that study, smokers were likewise found to have a 40% excess death rate, with 21% of all male deaths attributed to tobacco and with most of the excess deaths involving the same diseases. Although it may not be possible to quantify, the estimated health effects of smoking in the present study are likely to be underestimates, given that an appreciable proportion of smokers (especially light smokers) stopped after the baseline survey and that the effects of stopping are seen relatively quickly (at least in relation to lung cancer and CHD).[2] The reasons for stopping were not clearly known and may be due at least in part to cigarette rationing in China during the 1970s and, perhaps, also to smoking-related illness (particularly among old people, for the proportion of stopping was positively related to age).

In the present study, the RR of lung cancer among male smokers was 3.8, and smoking was responsible for about 63% of male lung cancer deaths. This is consistent with other studies in China during the 1980s,[16-19] but much lower than that reported in Western populations (typically a 20-fold RR of male lung cancer).[4] It may reflect the shorter duration of cigarette smoking and the relatively late age of starting to smoke in China (Table 2),[6,20] as well as, perhaps, the relatively high background rate of lung cancer not related to smoking.[21-23] No information was collected in the present study about exposures to domestic air pollution (such as cooking, heating, and passive smoking). Nor were the effects of exposure to industrial air pollution assessed, although these are likely to be negligible, given the types of factories studied and the similarity of the nonsmoker lung cancer rates to those of another prospective study in a nonoccupational population from Shanghai.[16]

The average lung cancer mortality rate in middle age (35-69 years) among lifelong nonsmokers in the United States (8/100 000)[24] is about one third of the rate observed in these studies in China. So, although the RR of lung cancer among Chinese smokers is currently much lower than that among Western smokers, the absolute risk of lung cancer from smoking in China is already large. Moreover, the mean cigarette consumption by Chinese men increased more than 2-fold between 1972 and 1992 (from 4 per man per day to 10 per man per day),[4] and there is evidence that smokers are starting at earlier ages.[25] The male lung cancer incidence rate among Shanghai men during the 1980s was already about two thirds of that in the United States.[16] The high background risk among male Chinese nonsmokers may be reduced substantially in the future (eg, by limiting indoor air pollution from cooking and heating).[21,22] But, if they are not, then a combination of the high smoking prevalence, the increasing RR due to the effects of more prolonged smoking, and the high background rate means that tobacco-attributable lung cancer mortality rates in China may soon exceed those now seen in the United States.

Tobacco is an important cause of esophageal cancer in Western populations, but its role in Chinese populations is still poorly understood.[26] In some rural areas of China where esophageal cancer is relatively common, smoking does not yet appear to play a major role.[27,28] By contrast, studies in lower-risk areas of China have, as in the present study, reported significant associations between cigarette smoking and esophageal cancer.[29-31] Most studies of possible associations between cigarette smoking and liver cancer were conducted in Western populations where liver cancer rates are extremely low and alcoholic cirrhosis may be of greater relative importance than in China, and the results have been inconsistent.[32-35] In China the liver cancer rate is high and is strongly related to lifelong hepatitis B virus infection and probably also to exposure to aflatoxins in foodstuffs.[36] In the present study, smoking was associated with a marginally significant 2-fold increase in the risk of liver cancer deaths, which was independent of alcohol consumption. Similar findings have been reported in other studies in Chinese populations.[16,37] If this association is causal, it could be of particular public health importance in China since liver cancer is already a major cause of death.

Cigarette smoking is an important cause of CHD in Western populations,[1,2,5,38-41] and the present study indicates that cigarette smoking is also a risk factor in China, where the mortality rate from the disease is low. This result is consistent with other studies in China[16,42,43] and Japan.[44] By contrast, although smoking has been shown to be a risk factor for stroke in Western populations, particularly in middle age,[2,41,45-50] there was no clear association between stroke and cigarette smoking in this Chinese population, despite high stroke rates. Similarly, in the other Shanghai prospective study,[16] no significant association was found between

Table 2.—Relative Risks (RRs) and 95% Confidence Intervals (CIs) of Lung Cancer in Relation to the Age of Starting Smoking Among Men*

Smoking Status at Baseline	RR (95% CI)		
		Age Started Smoking	
	Nonsmoker	≥25 y	<25 y
Nonsmoker	1.0 (0.6-1.7)	...	...
1-19 Cigarettes per d	...	2.2 (1.4-3.4)†	4.3 (2.6-7.2)‡
≥20 Cigarettes per d	...	2.5 (1.4-4.5)§	9.2 (6.2-13.5)‡

*The RRs were estimated in a Cox proportional hazards model, stratified for factories, and adjusted for age at baseline. The risk of lung cancer among nonsmokers was used as a reference group. The 95% CIs for RRs were estimated by floating absolute risks methods, which ascribe some variation to the results for the reference group of nonsmokers. Ellipses indicate data not applicable.
†P=.01 for comparison with nonsmoker category.
‡P<.001 for comparison with nonsmoker category.
§P=.03 for comparison with nonsmoker category.

Table 3.—Age-Standardized Annual Mortality Rates and Relative Risks (RRs) by Smoking Status at Baseline Among Women

Cause of Death (*ICD-9* Code)*	No. of Deaths	Mortality per 100 000 Persons		RR (95% Confidence Interval) Among Smokers‡	z Values	P Values§
		Nonsmoker at Baseline (45 685†‡)	Current Smoker at Baseline (3409†)			
All neoplastic (140-239)	82	170	143	0.9 (0.4-1.9)	−0.26	.80
All vascular (390-459)	76	139	255	2.1 (1.2-3.7)	2.47	.01
All respiratory (460-519)	14	14	123	10.7 (3.4-33.2)	4.09	<.001
Other causes§	35	69	89	1.2 (0.5-3.3)	0.43	.67
All causes	207	393	627	1.7 (1.2-2.5)	2.82	.005

**ICD-9* indicates *International Classification of Diseases, Ninth Edition.*
†Observed person-years.
‡The RRs were estimated in a Cox proportional hazards model, stratified for factories and adjusted for age systolic blood pressure, serum cholesterol, and regular alcohol drinking (yes vs no) at baseline.
§Including 7 deaths with unknown causes.

smoking and stroke death. About 40% of incident stroke cases in China are due to hemorrhage,[51-53] which is about 3 times the proportion reported in many Western populations, and hemorrhagic strokes have a higher case-fatality rate than ischemic strokes. If the association of smoking is mainly with ischemic strokes,[50] this may explain, at least in part, the apparent lack of association between cigarette smoking and total stroke mortality in this Chinese population.

Although the background rates of COPD are low in Western populations, cigarette smoking still causes large numbers of deaths from the disease since the RRs are high (≥10).[2,54-57] In China the background rates in nonsmokers are substantial, particularly in rural areas. So, although the RR may currently be only 2-fold, the absolute death rate from tobacco-related COPD is probably already larger in China than in the West.

In summary, the present results confirm that cigarette smoking is a major cause of death in China and that, in middle-aged Shanghai men, about one fifth of all deaths are caused by cigarette smoking. The current health effects of smoking, however, chiefly reflect the consequences of past smoking patterns, and the future health effects of current smoking patterns are likely to become much larger, given the recent large increase in cigarette consumption, particularly at younger ages, in China.[4,6,25]

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