

Association Between Exclusive Pipe Smoking and Mortality From Cancer and Other Diseases

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Background: Although many studies have examined the adverse health effects of pipe smoking combined with other forms of tobacco use, few have included large numbers of exclusive pipe smokers. The prevalence of pipe smoking has declined since the 1960s, yet usage is still common regionally, especially among older populations. **Methods:** Using Cox proportional hazards models, we examined the association between pipe smoking and mortality from tobacco-related cancers and other diseases in a cohort of U.S. men enrolled in the Cancer Prevention Study II, an American Cancer Society prospective study. The cohort of 138 307 men included those who reported, in their 1982 enrollment questionnaire, exclusive current or former use of pipes (n = 15 263 men) or never use of any tobacco product (n = 123 044 men). Analyses were based on 23 589 men who died during 18 years of follow-up. **Results:** Current pipe smoking, compared with never use of tobacco, was associated with an increased risk of death from cancers of the lung (relative risk [RR] = 5.00, 95% confidence interval [CI] = 4.16 to 6.01), oropharynx (RR = 3.90, 95% CI = 2.15 to 7.08), esophagus (RR = 2.44, 95% CI = 1.51 to 3.95), colorectum (RR = 1.41, 95% CI = 1.15 to 1.73), pancreas (RR = 1.61, 95% CI = 1.24 to 2.09), and larynx (RR = 13.1, 95% CI = 5.2 to 33.1), and from coronary heart disease (RR = 1.30, 95% CI = 1.18 to 1.43), cerebrovascular disease (RR = 1.27, 95% CI = 1.09 to 1.48), and chronic obstructive pulmonary disease (RR = 2.98, 95% CI = 2.17 to 4.11). These risks were generally smaller than those associated with cigarette smoking and similar to or larger than those associated with cigar smoking. Relative risks of lung cancer showed statistically significant increases with number of pipes smoked per day, years of smoking, and depth of inhalation and decreases with years since quitting. **Conclusion:** Results from this large prospective study suggest that pipe smoking confers a risk of tobacco-associated disease similar to cigar smoking. [J Natl Cancer Inst 2004;96:853-61]

Clinical reports as early as 1795 linked pipe smoking with carcinoma of the lip and tongue, as noted by Doll (1). However, the risks associated with the exclusive use of pipes have been difficult to study because pipes are the least commonly used tobacco product in the United States (2), and relatively few smokers use pipes exclusively. Traditionally, men in the United States have either switched from cigarettes to pipes or smoked pipes in combination with cigarettes or cigars (3).

The prevalence of pipe smoking among adult men in the United States has decreased from 14.1% in 1965 to 2.0% in 1991 (4), and pipe smoking remains rare among U.S. women (<0.1% in 1991) (4). The prevalence of pipe smoking is highest among men aged 45 or older and in the Midwest (4). Pipes are commonly used by some populations, including

American Indians (male prevalence = 6.9% in 1991) (5) and by both men and women in parts of China (20% prevalence in 1996) (6). The National Youth Tobacco Survey has measured prevalence of pipe smoking among U.S. youth since 1999. The prevalence of current pipe smoking has increased from 2.4% to 3.5% of middle school students and from 2.8% to 3.2% of high school students from 1999 to 2002; prevalence was higher among boys than girls and varied by state and ethnicity (7,8).

Exclusive pipe smoking has been positively associated with tobacco-related diseases in prospective (9-12) and case-control studies (13-23). The cohorts have contributed greatly to the epidemiologic evidence on tobacco and disease and include the Hammond-Horn nine-state study (9), the U.S. Veterans' study (10), a sample of the Swedish population (11), and the Norwegian Cardiovascular Study (12). However, these studies have generally reported wide confidence intervals for the relative risk (RR) estimates associated with exclusive pipe smoking and have not been able to stratify by pipe smoking characteristics such as amount or duration because of small sample size. Case-control studies generally have not distinguished between current and former pipe smoking and present results for "ever" pipe smokers. Most published studies, especially prospective studies, have adjusted only for age and have not considered potentially important covariates such as socioeconomic status and alcohol use.

To provide a more precise estimate of the risks associated with pipe smoking, we analyzed data on a large number of exclusive pipe smokers (both current and former) from the Cancer Prevention Study II (CPS-II), an American Cancer Society prospective cohort study. We analyzed the risks of nine cancers known to be associated with tobacco as well as several other tobacco-related diseases, adjusting for potential confounding factors.

SUBJECTS AND METHODS

The CPS-II is an ongoing prospective cohort of approximately 1.2 million U.S. adults (676 306 women and 508 351 men) begun in the fall of 1982 (24,25). American Cancer Society (ACS) volunteers asked their friends, neighbors, and acquaintances who were at least 30 years old to participate in the study. Each participant completed a confidential, four-page mailed questionnaire on their smoking habits, alcohol intake, educa-

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See "Notes" following "References."

DOI: 10.1093/jnci/djh144

Journal of the National Cancer Institute, Vol. 96, No. 11, © Oxford University Press 2004, all rights reserved.

Table 1. Demographic and other characteristics of CPS-II men who, at enrollment in 1982, reported either never use of tobacco products or exclusive smoking of pipes

Characteristic	Pipe smoking status		
	Never, No. (%)	Current, No. (%)	Former, No. (%)
Total	123 044 (89.0)	8880 (6.4)	6383 (4.6)
Median age at enrollment	56	58	59
Range of age at enrollment	30–102	30–96	30–99
Race			
White	115 113 (93.6)	8488 (95.6)	6194 (97.0)
Nonwhite	7931 (6.4)	392 (4.4)	189 (3.0)
Educational level			
Less than high school	14 028 (11.4)	851 (9.6)	397 (6.2)
High school graduate	22 524 (18.3)	1477 (16.6)	717 (11.2)
Some college	28 841 (23.4)	2147 (24.2)	1434 (22.5)
College graduate	24 023 (19.5)	1852 (20.9)	1482 (23.2)
Graduate school	32 050 (26.0)	2462 (27.7)	2308 (36.2)
Missing	1578 (1.3)	91 (1.0)	45 (0.7)
Current alcohol consumption, No. of drinks per day			
Abstainer	28 337 (23.0)	971 (10.9)	770 (12.1)
<1	15 504 (12.6)	1282 (14.4)	1111 (17.4)
1	6850 (5.6)	790 (8.9)	617 (9.7)
2–3	7107 (5.8)	975 (11.0)	627 (9.8)
≥4	3787 (3.1)	520 (5.9)	295 (4.6)
Missing all information	44 085 (35.8)	2715 (30.6)	1881 (29.5)
Unquantifiable	17 374 (14.1)	1627 (18.3)	1082 (17.0)
BMI, kg/m ²			
<18.5	995 (0.8)	82 (0.9)	40 (0.6)
18.5–24.9	48 440 (39.4)	3863 (43.5)	2706 (42.4)
25.0–29.9	58 745 (47.7)	4072 (45.9)	3053 (47.8)
≥30.0	12 182 (9.9)	704 (7.9)	480 (7.5)
Missing	2682 (2.2)	159 (1.8)	104 (1.6)
Reported prevalent disease at enrollment			
Cancer (except nonmelanoma skin)	5091 (4.1)	343 (3.9)	323 (5.1)
Heart disease or diabetes	15 593 (12.7)	1109 (12.5)	968 (15.2)
Stroke	1652 (1.3)	124 (1.4)	99 (1.6)
Emphysema or chronic bronchitis	2792 (2.3)	208 (2.3)	185 (2.9)
Any of the above	22 676 (18.4)	1596 (18.0)	1396 (21.9)

tional level, and other characteristics. This cohort is more likely to be college-educated, married, middle-class, and white than the general U.S. population (26). Informed consent to participate in the study was implied by the return of the self-administered questionnaire. All aspects of the CPS-II study protocol have been reviewed and approved by the Emory University Institutional Review Board and are renewed annually.

Information on pipe smoking was based on questionnaire responses in 1982 and was not updated during the follow-up. Men were asked “Do you now or have you ever smoked cigarettes, cigars or pipes at least one a day for one year’s time?” Current and former pipe smoking habits were assessed by asking the number of pipes smoked a day, age at which pipe smoking began, total years of pipe smoking, and depth of inhalation of pipe smoking. Former pipe smokers were asked their age at smoking cessation. Men were also asked about the use of smokeless tobacco (chewing tobacco and snuff). Users of cigarettes, cigars, or smokeless tobacco were excluded from this analysis. Women could not be included in this analysis because they were not asked whether they smoked pipes.

The vital status and cause of death of participants in CPS-II have been ascertained biennially since the month of enrollment by two methods: until 1988, via personal inquiries from ACS volunteers in September 1984, 1986, and 1988, with reported deaths verified by death certificate; since 1988, through automated linkage with the National Death Index (NDI) (27). As of December 31, 2000, 34.6% of men had died, 65.2% were still living, and 0.2% had follow-up censored on September 1, 1988,

because of insufficient data for linkage with the NDI. Death certificates or multiple cause-of-death codes were obtained for 98.9% of all deaths. The underlying cause of death was coded according to the *International Classification of Diseases*, Ninth Revision (ICD-9) (28).

Person-years at risk were accrued from month of enrollment through the end of follow-up (December 31, 2000), the date of death, or the date lost to follow-up (because of insufficient information for NDI linkage), whichever occurred first. Age-standardized death rates were directly standardized to the age distribution of person-years among CPS-II men during the 18 years of follow-up (29).

For the purpose of this study, we restricted the cohort to the 138 307 men who reported either exclusive use of pipes (n = 15 263) or never use of any tobacco product (n = 123 044). We examined both all-cause mortality and cause-specific mortality for diseases related to cigarette smoking (30,31). The causes of interest included several cancers (lung, oropharynx, esophagus, larynx, stomach, colorectal, pancreas, bladder, and kidney), cardiovascular disease (coronary heart disease and stroke), and chronic obstructive pulmonary disease. Men who reported prevalent disease at enrollment in 1982 were excluded as follows: analyses of cancer mortality excluded men who reported any prevalent cancer except nonmelanoma skin cancer; analysis of coronary heart disease mortality excluded men who reported prevalent heart disease or diabetes; analysis of cerebrovascular disease mortality excluded men who reported prevalent stroke; and analysis of

Table 2. Mortality rates, hazard ratios (HRs), and 95% confidence intervals (CIs) comparing men who never used any tobacco product with those who smoked pipes exclusively, CPS-II, 1982–2000

Cause of death (ICD-9 codes)	Pipe-smoking status	No. of deaths	Rate*	Age-adjusted HR (95% CI)†	Multivariable-adjusted HR (95% CI)‡
All causes§	Never	20 620	1295.2	1.00 (referent)	1.00 (referent)
	Current	1883	1648.9	1.28 (1.22 to 1.34)	1.33 (1.27 to 1.39)
	Former	1086	1216.8	0.94 (0.89 to 1.00)	1.00 (0.94 to 1.06)
Oropharynx cancer (140–149)	Never	50	2.6	1.00 (referent)	1.00 (referent)
	Current	15	10.8	3.93 (2.19 to 7.08)	3.90 (2.15 to 7.08)
	Former	3	2.6	1.09 (0.34 to 3.50)	1.19 (0.37 to 3.87)
Esophagus cancer (150)	Never	113	6.0	1.00 (referent)	1.00 (referent)
	Current	20	14.4	2.47 (1.53 to 3.97)	2.44 (1.51 to 3.95)
	Former	10	9.3	1.58 (0.83 to 3.02)	1.60 (0.83 to 3.09)
Stomach cancer (151)	Never	225	11.7	1.00 (referent)	1.00 (referent)
	Current	18	12.9	1.11 (0.69 to 1.79)	1.15 (0.71 to 1.87)
	Former	10	8.9	0.78 (0.41 to 1.47)	0.84 (0.45 to 1.59)
Colorectal cancer (153–154)	Never	1035	54.1	1.00 (referent)	1.00 (referent)
	Current	104	75.0	1.39 (1.13 to 1.70)	1.41 (1.15 to 1.73)
	Former	48	44.4	0.82 (0.61 to 1.09)	0.87 (0.65 to 1.16)
Pancreas cancer (157)	Never	554	29.1	1.00 (referent)	1.00 (referent)
	Current	64	45.9	1.58 (1.22 to 2.05)	1.61 (1.24 to 2.09)
	Former	25	22.7	0.80 (0.53 to 1.19)	0.80 (0.53 to 1.20)
Larynx cancer (161)	Never	9	0.5	1.0 (referent)	1.0 (referent)
	Current	10	7.2	15.2 (6.2 to 37.5)	13.1 (5.2 to 33.1)
	Former	3	2.5	5.8 (1.6 to 21.5)	5.6 (1.5 to 21.2)
Lung cancer (162)	Never	447	23.3	1.00 (referent)	1.00 (referent)
	Current	160	114.9	4.92 (4.10 to 5.89)	5.00 (4.16 to 6.01)
	Former	40	36.8	1.56 (1.13 to 2.16)	1.70 (1.23 to 2.36)
Bladder cancer (188)	Never	176	9.2	1.00 (referent)	1.00 (referent)
	Current	20	14.3	1.58 (1.00 to 2.51)	1.50 (0.94 to 2.39)
	Former	18	15.6	1.76 (1.08 to 2.86)	1.68 (1.03 to 2.75)
Kidney cancer (189)	Never	226	12.0	1.00 (referent)	1.00 (referent)
	Current	14	10.0	0.85 (0.49 to 1.45)	0.91 (0.53 to 1.57)
	Former	13	12.1	1.04 (0.59 to 1.82)	1.17 (0.67 to 2.06)
Coronary heart disease (410–414)¶	Never	5602	322.8	1.00 (referent)	1.00 (referent)
	Current	481	389.9	1.22 (1.11 to 1.33)	1.30 (1.18 to 1.43)
	Former	305	311.0	0.96 (0.85 to 1.07)	1.04 (0.93 to 1.17)
Cerebrovascular disease (430–438)#	Never	2138	104.3	1.00 (referent)	1.00 (referent)
	Current	178	125.5	1.21 (1.04 to 1.41)	1.27 (1.09 to 1.48)
	Former	118	95.7	0.93 (0.77 to 1.12)	1.00 (0.83 to 1.20)
Chronic obstructive pulmonary disease (490–492, 496)**	Never	245	12.0	1.00 (referent)	1.00 (referent)
	Current	46	32.7	2.74 (2.00 to 3.75)	2.98 (2.17 to 4.11)
	Former	16	13.0	1.12 (0.67 to 1.85)	1.35 (0.81 to 2.25)

*Death rates are per 100 000 person-years and are age-standardized to the CPS-II male person-year distribution. ICD-9 = *International Classification of Diseases*, 9th edition.

†From Cox proportional hazards models, adjusted for age only.

‡From Cox proportional hazards models, adjusted for age, race, educational level, body mass index, and alcohol consumption.

§Analysis for all causes excluded men who reported prevalent cancer, heart disease, diabetes, stroke, emphysema, or chronic bronchitis in 1982.

||Analyses for cancers excluded men who reported any prevalent cancer in 1982.

¶Analysis for coronary heart disease excluded men who reported prevalent heart disease or diabetes in 1982.

#Analysis for cerebrovascular disease excluded men who reported prevalent stroke in 1982.

**Analysis for chronic obstructive pulmonary disease excluded men who reported prevalent emphysema or chronic bronchitis in 1982.

chronic obstructive pulmonary disease mortality excluded men who reported prevalent chronic bronchitis or emphysema. The analysis of all-cause mortality excluded men who reported a history of any of these diseases at enrollment.

Statistical Analysis

We used Cox proportional hazards models to estimate hazard ratios and 95% confidence intervals for mortality associated with pipe smoking and to adjust for other potential risk factors reported at baseline (32). We assessed the appropriateness of the Cox proportional hazards model for each cause of death by

plotting log(–log) survival curves against survival time. The log(–log) survival curves were essentially parallel, suggesting that the proportional hazards assumption was met. All statistical tests were two-sided; hazard ratios were considered statistically significantly elevated if the lower limit of the 95% confidence interval was greater than 1.0, and *P* values less than .05 were considered statistically significant. Indicator variables were used for all independent variables. All models were adjusted for single year of age by stratification. Multivariable Cox proportional hazards models were adjusted for current alcohol consumption (none, <1 drink daily, 1 drink daily, 2–3 drinks daily,

Table 3. Mortality hazard ratios (HRs) and 95% confidence intervals (CIs) comparing exclusive current pipe smokers with men who never used any tobacco product, by pipes smoked per day, duration of smoking, and inhalation, CPS-II, 1982–2000*

Smoking habit (N)†	Lung cancer		Esophagus cancer		Stomach cancer		Colorectal cancer			
	No. of deaths	HR (95% CI)‡	No. of deaths	HR (95% CI)‡	No. of deaths	HR (95% CI)‡	No. of deaths	HR (95% CI)‡		
Never smokers	447	1.00 (referent)	113	1.00 (referent)	225	1.00 (referent)	1035	1.00 (referent)		
No. of pipes smoked per day										
1–3 (2485)	} 1–6	16	1.99 (1.21 to 3.29)	5†	} 2.41 (1.25 to 4.62)	7†	} 1.11 (0.57 to 2.17)	24	} 1.29 (0.86 to 1.94)	
4–6 (2187)		42	5.23 (3.80 to 7.20)	5		2		27		1.43 (0.97 to 2.10)
7–10 (2044)		51	6.61 (4.93 to 8.86)	7†		5†		22		1.24 (0.81 to 1.89)
≥11 (1317)	} 7+	36	7.67 (5.44 to 10.81)	2	2.85 (1.44 to 5.67)	2	1.19 (0.56 to 2.53)	22	1.99 (1.30 to 3.04)	
<i>P</i> _{trend} #			<.001		.399		.947		.103	
Duration, y										
1–24 (1948)	} 1–44	14	3.17 (1.85 to 5.42)	2†	} 1.48 (0.72 to 3.05)	2†	} 0.64 (0.28 to 1.44)	14	} 1.33 (0.79 to 2.27)	
25–34 (2140)		21	3.87 (2.48 to 6.04)	0†		1†		16		1.24 (0.75 to 2.04)
35–44 (2368)		56	5.66 (4.25 to 7.55)	6		3		26		1.20 (0.81 to 1.78)
≥45 (1522)	45+	56	6.48 (4.84 to 8.68)	7	3.73 (1.69 to 8.22)	10	2.21 (1.15 to 4.22)	36	1.71 (1.22 to 2.40)	
<i>P</i> _{trend} #			.003		.091		.005		.635	
Inhalation										
None (5243)	none	52	2.85 (2.13 to 3.81)	9	1.84 (0.93 to 3.66)	9	0.99 (0.51 to 1.94)	71	1.64 (1.29 to 2.10)	
Slight (1741)	} some	49	8.05 (5.97 to 10.84)	7†	} 3.19 (1.55 to 6.58)	3†	} 1.45 (0.68 to 3.09)	16	} 1.20 (0.73 to 1.97)	
Moderate/deep (1091)		42	11.06 (8.03 to 15.23)	1		4		11		1.24 (0.68 to 2.25)
<i>P</i> _{trend} #			<.001		.222		.589		.256	

*From Cox proportional hazards models, adjusted for age, race, educational level, body mass index, and alcohol consumption. — = risks were not estimated for categories with 0 deaths.

†Number in category is based on current smokers before exclusions for prevalent disease; categories may not sum to total because of missing values. For outcomes with fewer than 20 deaths among current smokers, categories have been dichotomized as follows: number of pipes smoked per day as 1–6 and ≥7; duration of smoking as 1–44 and ≥45 years; inhalation as none and some.

‡Analyses for cancers excluded men who reported any prevalent cancer in 1982.

§Analysis for coronary heart disease excluded men who reported prevalent heart disease or diabetes in 1982.

||Analysis for cerebrovascular disease excluded men who reported prevalent stroke in 1982.

¶Analysis for chronic obstructive pulmonary disease excluded men who reported prevalent emphysema or chronic bronchitis in 1982.

#*P*_{trend} was evaluated by using a likelihood ratio test and is based on current pipe smokers only (does not include referent).

4 or more drinks daily, and unquantifiable use), educational level (less than high school graduate, high school graduate, some college or vocational school, college graduate, and graduate school), race (white and nonwhite), and body mass index (normal or below [$<25 \text{ kg/m}^2$], overweight [$25\text{--}29 \text{ kg/m}^2$], and obese [$\geq 30 \text{ kg/m}^2$]). Men who left all alcohol questions blank (“missing” alcohol use) were combined with men who reported no current alcohol consumption based on a previous analysis of CPS-II (33) in which these two groups were shown to have similar mortality patterns. In models for coronary heart disease mortality, we assessed other potential confounding factors, including occupation, current employment, vegetable and fruit consumption, dietary fat consumption, and aspirin use; these factors had little effect on the risk estimates (data not shown) and were not included in final models.

Current pipe smokers were further characterized by number of pipes smoked per day, years of smoking, and depth of inhalation, and former pipe smokers were characterized by number of years since quitting smoking and age at quitting smoking. Causes of death with fewer than 15 deaths among current or former smokers are not shown by smoking characteristic. Linear trends of smoking characteristics, excluding lifelong nonusers, were tested using the likelihood ratio test (34).

Epidemiologic evidence suggests synergism between tobacco smoking and alcohol consumption for cancers of the upper aero-digestive tract, which includes the oropharynx, esophagus, and larynx (30). Therefore we examined the joint association of pipe smoking and alcohol consumption with cancers of the

upper aero-digestive tract. Men with unquantifiable alcohol consumption were excluded from this analysis. A likelihood ratio test was used to test for multiplicative interaction between pipe smoking and alcohol consumption.

Analyses of cigarette smoking in CPS-II generally use only the first 6 years of follow-up to minimize the effects of misclassification among current smokers who quit smoking during more prolonged follow-up (35). We chose to use 18 years of follow-up to maximize the number of deaths available for analysis. To examine the effect of cessation of pipe smoking over the 18-year follow-up, we compared relative risks for current and former pipe smoking associated with all causes, lung cancer, coronary heart disease, cerebrovascular disease, and chronic obstructive pulmonary disease for three six-year periods: 1982–1988; 1989–1994; and 1995–2000. If bias due to misclassification of smoking status was substantial, we would expect to see the relative risks of current smoking decrease over time. Temporal trends were tested by including interaction terms between survival time and smoking in the Cox model (36); statistical significance of interaction terms was evaluated using the Wald chi-square test.

RESULTS

Demographic and other characteristics of the study population according to pipe smoking status at baseline are presented in Table 1. Men who had formerly smoked pipes were more highly educated than men who currently smoked pipes or who had never used tobacco. Both current and former pipe smokers were

Table 3 (continued).

Pancreas cancer		Bladder cancer		Coronary heart disease		Cerebrovascular disease		Chronic obstructive pulmonary disease	
No. of deaths	HR (95% CI)‡	No. of deaths	HR (95% CI)‡	No. of deaths	HR (95% CI)§	No. of deaths	HR (95% CI)	No. of deaths	HR (95% CI)¶
554	1.00 (referent)	176	1.00 (referent)	5602	1.00 (referent)	2138	1.00 (referent)	245	1.00 (referent)
18	1.74 (1.08 to 2.78)	1†		115	1.24 (1.03 to 1.50)	42	1.21 (0.89 to 1.65)	8	2.27 (1.12 to 4.61)
19	1.87 (1.18 to 2.96)	7	1.19 (0.58 to 2.42)	124	1.25 (1.05 to 1.50)	50	1.34 (1.01 to 1.78)	14	3.32 (1.93 to 5.72)
14	1.45 (0.85 to 2.48)	6†		108	1.24 (1.02 to 1.50)	49	1.46 (1.10 to 1.94)	12	3.39 (1.89 to 6.08)
10	1.71 (0.92 to 3.21)	5	2.03 (1.10 to 3.76)	81	1.47 (1.18 to 1.83)	16	0.82 (0.50 to 1.34)	9	4.05 (2.07 to 7.91)
	.694		.431		.659		.304		.563
14	2.49 (1.46 to 4.25)	1†		54	1.26 (0.96 to 1.65)	17	1.18 (0.73 to 1.91)	0	—
11	1.55 (0.85 to 2.84)	2†		68	1.29 (1.01 to 1.64)	18	1.09 (0.69 to 1.74)	2	1.19 (0.29 to 4.82)
17	1.34 (0.82 to 2.18)	4	0.90 (0.42 to 1.92)	129	1.26 (1.05 to 1.50)	49	1.37 (1.03 to 1.82)	10	2.63 (1.38 to 4.99)
12	1.16 (0.65 to 2.07)	12	2.81 (1.54 to 5.14)	179	1.37 (1.18 to 1.59)	67	1.15 (0.90 to 1.47)	29	4.49 (3.02 to 6.67)
	.233		.046		.027		.741		<.001
34	1.43 (1.01 to 2.02)	7	0.88 (0.41 to 1.88)	251	1.18 (1.03 to 1.34)	114	1.39 (1.15 to 1.69)	18	2.13 (1.31 to 3.46)
8	1.13 (0.56 to 2.28)	6†		101	1.54 (1.26 to 1.87)	25	1.07 (0.72 to 1.59)	15	5.33 (3.15 to 9.02)
15	3.33 (1.99 to 5.57)	5	2.86 (1.55 to 5.30)	69	1.61 (1.27 to 2.04)	12	0.77 (0.44 to 1.36)	9	5.10 (2.61 to 9.98)
	.040		.059		.013		.027		.022

more likely to report alcohol consumption than never users of tobacco.

Table 2 presents death rates, adjusted for age, and hazard ratios, adjusted for age and other potentially confounding variables, comparing current and former pipe smokers with never tobacco users. Current pipe smokers experienced statistically significantly higher death rates than never users from all causes (RR = 1.33, 95% CI = 1.27 to 1.39); from cancers of the larynx (RR = 13.1, 95% CI = 5.2 to 33.1), lung (RR = 5.00, 95% CI = 4.16 to 6.01), oropharynx (RR = 3.90, 95% CI = 2.15 to 7.08), esophagus (RR = 2.44, 95% CI = 1.51 to 3.95), colorectum (RR = 1.41, 95% CI = 1.15 to 1.73), and pancreas (RR = 1.61, 95% CI = 1.24 to 2.09); from chronic obstructive pulmonary disease (RR = 2.98, 95% CI = 2.17 to 4.11); from cerebrovascular disease (RR = 1.27, 95% CI = 1.09 to 1.48); and from coronary heart disease (RR = 1.30, 95% CI = 1.18 to 1.43). Current pipe smokers also had statistically nonsignificant increases in death from cancers of the stomach (RR = 1.15, 95% CI = 0.71 to 1.87) and bladder (RR = 1.50, 95% CI = 0.94 to 2.39). No association was observed between current pipe smoking and kidney cancer mortality. Former pipe smokers experienced smaller increases in risk from most of these diseases, including cancers of the larynx (RR = 5.6, 95% CI = 1.5 to 21.2), lung (RR = 1.70, 95% CI = 1.23 to 2.36), oropharynx (RR = 1.19, 95% CI = 0.37 to 3.87), esophagus (RR = 1.60, 95% CI = 0.83 to 3.09), bladder (RR = 1.68, 95% CI = 1.03 to 2.75); and chronic obstructive pulmonary disease (RR = 1.35, 95% CI = 0.81 to 2.25).

Trends in multivariable-adjusted relative risks associated with current pipe smoking were evident in relation to the number of pipes smoked per day, duration of pipe smoking, and depth of inhalation (Table 3). The relative risk for death from lung cancer increased from 1.99 for men who smoked 1–3 pipes daily to 7.67 for men who smoked 11 or more pipes daily ($P_{\text{trend}} < .001$). Similar increases in lung cancer mortality risk were seen with the duration of smoking ($P_{\text{trend}} = .003$) and with depth of inhalation ($P_{\text{trend}} < .001$). Statistically significant increasing dose

response trends were observed with years of smoking for coronary heart disease, chronic obstructive pulmonary disease, and stomach and bladder cancers and with depth of inhalation for coronary heart disease, chronic obstructive pulmonary disease, and pancreas cancer. We observed an anomalous inverse association with depth of inhalation for cerebrovascular disease that we cannot explain.

We also analyzed the relative risks of death from tobacco-associated diseases among former pipe smokers by years since quitting pipe smoking and age at quitting (Table 4). For most diseases, the relative risk decreased with years since quitting and with younger age at quitting. The relative risk among former pipe smokers was intermediate between that of current smokers and never tobacco users in most categories of amount, duration, and depth of inhalation (data not shown).

We assessed the potential synergism between pipe smoking and alcohol consumption for cancers of the upper aero-digestive tract (Table 5). The highest relative risk estimate was seen in men who reported current pipe smoking and drinking four or more drinks per day (RR = 15.1, 95% CI = 5.9 to 39.0) compared with men who use neither tobacco nor alcohol ($P_{\text{interaction}} = .013$).

To examine the effect of cessation of pipe smoking over the 18-year follow-up period, we compared the relative change in death rates among current and former pipe smokers compared with never tobacco users over three 6-year periods of follow-up (Table 6). Among current pipe smokers, no statistically significant trends in the relative risks of death from all causes or from any of the specific causes were evident with increasing follow-up. Among former smokers, there was a statistically significant decrease in the risk of death from lung cancer with increasing length of follow-up but also a statistically significant increase in the risk of death from cerebrovascular disease. Generally, the estimates obtained from 18 years of follow-up were similar to but more stable than those from 6 years of follow-up.

We compared the relative mortality risk estimates from smoking-attributable diseases associated with exclusive current

Table 4. Mortality hazard ratios (HRs) and 95% confidence intervals (CIs) comparing former pipe smokers with men who never used any tobacco product, by years since quitting and age at quitting, CPS-II, 1982–2000*

Smoking habit (N) [†]	Lung cancer		Colorectal cancer		Pancreas cancer		Bladder cancer	
	No. of deaths	HR (95% CI) [‡]	No. of deaths	HR (95% CI) [‡]	No. of deaths	HR (95% CI) [‡]	No. of deaths	HR (95% CI) [‡]
Never smokers	447	1.00 (referent)	1035	1.00 (referent)	554	1.00 (referent)	176	1.00 (referent)
Years since quitting								
<10 (2569)	22	2.49 (1.62 to 3.83)	24	1.18 (0.79 to 1.77)	10	0.86 (0.46 to 1.61)	8	1.97 (0.96 to 4.02)
≥10 (3580)	15	1.05 (0.63 to 1.76)	20	0.62 (0.40 to 0.96)	14	0.76 (0.44 to 1.29)	10	1.55 (0.82 to 2.95)
<i>P</i> _{trend} [#]		.003		.052		.843		.563
Age at quitting, y								
≥45 (2984)	33	2.30 (1.61 to 3.30)	35	1.05 (0.75 to 1.47)	16	0.85 (0.52 to 1.40)	14	2.01 (1.16 to 3.49)
<45 (3170)	5	0.58 (0.24 to 1.40)	9	0.47 (0.24 to 0.90)	8	0.71 (0.35 to 1.42)	4	1.13 (0.42 to 3.06)
<i>P</i> _{trend} [#]		.006		.030		.952		.408

*From Cox proportional hazards models, adjusted for age, race, educational level, body mass index, and alcohol consumption.

[†]Number in category is based on former smokers before exclusions for prevalent disease; categories may not sum to total because of missing values.

[‡]Analyses for cancers excluded men who reported any prevalent cancer in 1982.

[§]Analysis for coronary heart disease excluded men who reported prevalent heart disease or diabetes in 1982.

^{||}Analysis for cerebrovascular disease excluded men who reported prevalent stroke in 1982.

[¶]Analysis for chronic obstructive pulmonary disease excluded men who reported prevalent emphysema or chronic bronchitis in 1982.

[#]*P*_{trend} was evaluated by using a likelihood ratio test and was based on former pipe smokers only (does not include referent).

pipe, cigarette, or cigar smoking among CPS-II men (Fig. 1). For most diseases, cigarette only smokers have the highest risk (37,38), and men who exclusively smoked pipes have risks that are similar to or higher than those associated with smokers of cigars only (39). The association between smoking and death from coronary heart disease does not differ by tobacco product (37,40).

DISCUSSION

Results from this large, prospective study provide more precise estimates of the relationship between pipe smoking and death from tobacco-attributable diseases than have been available previously. In this cohort, pipe smoking conferred a risk similar to or greater than that for cigar smoking for cancers of the lung, larynx, esophagus, and oropharynx and for coronary heart disease (39,40).

The epidemiologic literature on tobacco use, including pipe and cigar smoking, has been reviewed recently (30). Many of the studies included in that review combined pipe and cigar smokers; however, the studies that examined exclusive pipe smoking showed results similar to ours. Of the prospective studies, ours is the largest and the only one to adjust for risk factors other than age. Men who smoke pipes exclusively have higher risk of lung cancer than men who have never smoked in most published prospective (9–12,41,42) and case–control (13–17) studies. In our study, risk of lung cancer mortality in men was increased fivefold for current pipe smokers; this estimate is higher than that reported in two earlier U.S. cohorts (9,10) but is consistent with studies conducted in Europe (11,12,41,42). Like our study, two large European case–control studies (13,17) reported that lung cancer risk increased with years of pipe smoking, number of pipes smoked per day, and depth of inhalation and decreased with time since cessation of smoking.

Risk of death from laryngeal cancer was also strongly associated with current pipe smoking (RR = 13.1). To our knowledge, the association with laryngeal cancer has not previously been assessed among exclusive pipe smokers. Our estimates for death from cancers of the oropharynx (RR = 3.90) and esophagus (RR = 2.44) are consistent with those from other prospec-

tive studies, including Hammond–Horn (9), the U.S. Veterans' Study (10), and a Swedish cohort (11). A hospital-based case–control study in Beijing observed a fivefold increased risk of oral cancer incidence among both male and female ever pipe smokers (18).

The risk estimate for stomach cancer mortality in this study is slightly lower than that reported in two prospective studies (10,12) or in a previous analysis in CPS-II men (RR = 1.3, 95% CI = 0.8 to 2.2), which was based on 14 years of follow-up (43). The risk of colorectal cancer mortality was highest for men who reported several decades of smoking or smoking 11 or more pipes per day, similar to results observed among cigarette smokers in CPS-II (44). Although no association was observed between current pipe smoking and colon or rectal cancer mortality in the Swedish study (11), Heineman et al. (45) observed an increasing risk of colon and rectal cancer death with increasing number of pipes smoked per day in a 26-year follow-up of U.S. veterans.

Risk of pancreatic cancer mortality associated with pipe smoking was increased in the Swedish prospective study (11) but not in two other prospective studies—the U.S. Veterans' study (10) or the Norwegian Cardiovascular Study (12). A hospital-based case–control study by Muscat et al. (19) observed an increased risk for pancreatic cancer incidence associated with ever pipe smoking.

Two previous studies in U.S. cohorts (9,10) reported an association between pipe smoking and bladder cancer mortality similar to that seen in CPS-II (RR = 1.50); a relative risk of 4.0 was reported in the Swedish study (11). The largest study of bladder cancer, a pooled analysis of European case–control studies (20), reported statistically significantly higher risk with longer duration of pipe smoking, as was also observed in CPS-II. We did not find an association between pipe smoking and kidney cancer mortality, similar to the results of two case–control studies of kidney cancer incidence (22,23).

Finally, our estimates of risk for cardiovascular and pulmonary disease are similar to those reported in the large Swedish study (11) and are within the range reported by other prospective studies. A limitation of our study is that smoking habits were reported

Table 4 (continued).

Coronary heart disease		Cerebrovascular disease		Chronic obstructive pulmonary disease	
No. of deaths	HR (95% CI)§	No. of deaths	HR (95% CI)	No. of deaths	HR (95% CI)¶
5602	1.00 (referent)	2138	1.00 (referent)	245	1.00 (referent)
112	1.09 (0.90 to 1.31)	48	1.19 (0.89 to 1.59)	8	2.01 (0.99 to 4.08)
176	0.99 (0.85 to 1.16) .576	65	0.89 (0.70 to 1.14) .137	8	1.13 (0.55 to 2.29) .240
211	1.13 (0.98 to 1.30)	83	1.06 (0.85 to 1.32)	12	1.54 (0.86 to 2.76)
78	0.83 (0.67 to 1.04) .008	30	0.86 (0.60 to 1.24) .245	4	1.22 (0.45 to 3.31) .770

Table 5. Effect of alcohol consumption on the association between upper aero-digestive tract cancer and exclusive pipe smoking, CPS-II men, 1982–2000*

Pipe smoking status	Alcohol consumption, No. of drinks per day									
	None		<1		1–3		≥4		Overall	
	No. of deaths	HR (95% CI)†	No. of deaths	HR (95% CI)†	No. of deaths	HR (95% CI)†	No. of deaths	HR (95% CI)†	No. of deaths	HR (95% CI)†
Never	105	1.0 (referent)	22	1.1 (0.7 to 1.7)	12	0.6 (0.4 to 1.2)	11	2.3 (1.2 to 4.3)	150	1.0 (referent)
Former	8	2.0 (1.0 to 4.1)	1	0.6 (0.2 to 1.5)	1	0.5 (0.2 to 1.4)	3	6.7 (2.5 to 18.0)	13	1.6 (0.9 to 2.8)
Current	10	1.8 (0.9 to 3.4)	2	1.3 (0.5 to 2.9)	12	4.7 (1.8 to 11.9)	11	15.1 (5.9 to 39.0)	35	3.3 (2.3 to 4.8)
Overall	123	1.0 (referent)	25	1.0 (0.6 to 1.5)	25	1.0 (0.7 to 1.5)	25	3.9 (2.5 to 6.0)		

*Upper aero-digestive tract cancers include oropharynx, esophagus, and larynx (*International Classification of Diseases*, 9th edition [ICD-9] codes 140–150, 161). HR = hazard ratio; CI = confidence interval.

†Cox proportional hazards models are adjusted for age. $P_{\text{interaction}} = .013$, based on likelihood ratio test.

only at baseline. For diseases such as lung cancer, in which risk increases exponentially with duration of smoking (46), the relative risk estimate among continuing smokers would be ex-

pected to increase over time. However, we found that the association between lung cancer and current pipe smoking remained relatively constant over time (Table 6). The expected increase

Table 6. Mortality hazard ratios (HRs) and 95% confidence intervals (CIs) comparing men who never used any tobacco product with men who smoked only pipes, CPS-II men, by follow-up period*

Cause of death (ICD-9 codes)	Pipe smoking status	Follow-up 1982–1988		Follow-up 1989–1994		Follow-up 1995–2000		$P_{\text{trend}}\ddagger$
		No. of deaths	HR (95% CI)	No. of deaths	HR (95% CI)	No. of deaths	HR (95% CI)	
All causes‡	Never	3698	1.00 (referent)	7113	1.00 (referent)	9809	1.00 (referent)	
	Current	303	1.16 (1.03 to 1.31)	694	1.40 (1.29 to 1.52)	886	1.34 (1.25 to 1.43)	.252
	Former	189	1.00 (0.87 to 1.16)	344	0.92 (0.83 to 1.03)	553	1.05 (0.97 to 1.15)	.319
Lung cancer (162)§	Never	87	1.00 (referent)	160	1.00 (referent)	200	1.00 (referent)	
	Current	39	6.26 (4.25 to 9.22)	47	3.95 (2.84 to 5.50)	74	5.34 (4.07 to 7.07)	.991
	Former	19	4.62 (2.79 to 7.66)	10	1.15 (0.61 to 2.19)	11	1.02 (0.55 to 1.88)	.001
Coronary heart disease (410–414)	Never	1297	1.00 (referent)	1938	1.00 (referent)	2367	1.00 (referent)	
	Current	101	1.15 (0.94 to 1.41)	176	1.37 (1.17 to 1.60)	204	1.33 (1.15 to 1.54)	.303
	Former	78	1.16 (0.92 to 1.46)	100	0.99 (0.81 to 1.22)	127	1.02 (0.85 to 1.22)	.476
Cerebrovascular disease (430–438)¶	Never	403	1.00 (referent)	699	1.00 (referent)	1036	1.00 (referent)	
	Current	25	0.95 (0.64 to 1.44)	65	1.37 (1.06 to 1.77)	88	1.32 (1.06 to 1.64)	.435
	Former	12	0.59 (0.33 to 1.05)	35	0.89 (0.63 to 1.25)	71	1.21 (0.95 to 1.54)	.012
Chronic obstructive pulmonary disease (490–492, 496)#	Never	45	1.00 (referent)	79	1.00 (referent)	121	1.00 (referent)	
	Current	2	0.71 (0.17 to 2.96)	20	4.06 (2.46 to 6.69)	24	3.13 (2.01 to 4.89)	.177
	Former	3	1.52 (0.47 to 4.91)	1	0.26 (0.04 to 1.84)	12	2.01 (1.10 to 3.66)	.312

*From Cox proportional hazards models, adjusted for age, race, educational level, body mass index, and alcohol consumption. ICD-9 = *International Classification of Diseases*, 9th edition.

† P_{trend} is based on the Wald chi-square test.

‡Analysis for all causes excluded men who reported prevalent cancer, heart disease, diabetes, stroke, emphysema, or chronic bronchitis in 1982.

§Analysis for lung cancer excluded men who reported any prevalent cancer in 1982.

||Analysis for coronary heart disease excluded men who reported prevalent heart disease or diabetes in 1982.

¶Analysis for cerebrovascular disease excluded men who reported prevalent stroke in 1982.

#Analysis for chronic obstructive pulmonary disease excluded men who reported prevalent emphysema or chronic bronchitis in 1982.

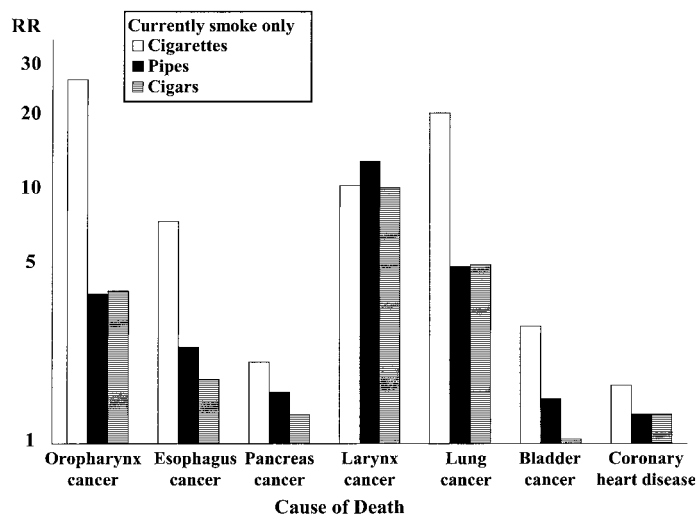


Fig. 1. Relative risk (RR) estimates for tobacco-attributable diseases associated with current exclusive cigarette, pipe, or cigar smoking among men in Cancer Prevention Study II (CPS-II). Estimates for pipe smoking are from Table 2. The associations between cigarette and cigar smoking and tobacco-attributable diseases in CPS-II men have been published previously (37–40). Estimates for the association between cigarette smoking and cancer of the oropharynx, esophagus, pancreas, larynx, and bladder are from the 1989 Surgeon General’s Report, p. 150 (38); those for lung cancer and coronary heart disease are from the 1997 National Cancer Institute Smoking and Tobacco Control: Monograph No. 8, p. 395, 400 (37). Estimates for the association between cigar smoking and cancer of the lung, oropharynx, esophagus, pancreas, larynx, and bladder are from Shapiro et al. (39); the estimate for coronary heart disease is from Jacobs et al. (40).

may have been obscured by misclassification of exposure due to cessation of smoking among current smokers during the 18-year follow-up period. The effect of this misclassification would be to underestimate the risks of continued smoking and to attenuate dose–response gradients. The main strength of our study was its size, which provided precise estimates of mortality risk associated with pipe smoking among men who smoked pipes exclusively and provided moderately stable estimates of risk for the more common endpoints in relation to the number of pipes smoked daily, duration of smoking, and depth of inhalation among current smokers, and age at quitting and years since quitting among former smokers. Comprehensively documenting the deleterious health effects of pipe smoking is important in countering efforts by the tobacco industry to promote pipes as a desirable alternative to cigarettes or cigars. The tobacco industry has repeatedly demonstrated its ability to create new markets by reviving interest in tobacco products that had appeared to have become obsolete, especially among youth and young adults. Two complementary approaches used to rekindle demand for products such as moist snuff, premium cigars, bidis, and hookah pipes are to minimize the adverse health consequences of these products by presenting them as a less hazardous alternative to cigarette smoking and to glamorize use by creating positive associations with celebrity, athleticism, success, and/or internationalism (47). Results from this large, prospective study strongly support a causal relationship between pipe smoking and mortality from cancers of the lung, larynx, esophagus, and oropharynx, and chronic obstructive pulmonary disease. Although the risk of dying from tobacco-associated diseases is lower for pipe smokers than for cigarette smokers, pipe smoking is as harmful as, and perhaps more harmful than, cigar smoking.

All tobacco products cause excessive morbidity and mortality. Our findings may help deter efforts by the tobacco industry to imply, directly or indirectly, as it has with smokeless tobacco (48,49) and low-yield cigarettes (50), that any tobacco product has negligible adverse health effects.

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NOTES

We are grateful to the 1.2 million American men and women who have participated in the Cancer Prevention Study II and to the American Cancer Society volunteers for their assistance in developing this cohort.

Manuscript received October 31, 2003; revised March 31, 2004; accepted April 6, 2004.