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## EFFECT OF CIGAR SMOKING ON THE RISK OF CARDIOVASCULAR DISEASE, CHRONIC OBSTRUCTIVE PULMONARY DISEASE, AND CANCER IN MEN

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### ABSTRACT

**Background** The sale of cigars in the United States has been increasing since 1993. Cigar smoking is a known risk factor for certain cancers and for chronic obstructive pulmonary disease (COPD). However, unlike the relation between cigarette smoking and cardiovascular disease, the association between cigar smoking and cardiovascular disease has not been clearly established.

**Methods** We performed a cohort study among 17,774 men 30 to 85 years of age at base line (from 1964 through 1973) who were enrolled in the Kaiser Permanente health plan and who reported that they had never smoked cigarettes and did not currently smoke a pipe. Those who smoked cigars (1546 men) and those who did not (16,228) were followed from 1971 through the end of 1995 for a first hospitalization for or death from a major cardiovascular disease or COPD, and through the end of 1996 for a diagnosis of cancer.

**Results** In multivariate analyses, cigar smokers, as compared with nonsmokers, were at higher risk for coronary heart disease (relative risk, 1.27; 95 percent confidence interval, 1.12 to 1.45), COPD (relative risk, 1.45; 95 percent confidence interval, 1.10 to 1.91), and cancers of the upper aerodigestive tract (relative risk, 2.02; 95 percent confidence interval, 1.01 to 4.06) and lung (relative risk, 2.14; 95 percent confidence interval, 1.12 to 4.11), with evidence of dose-response effects. There appeared to be a synergistic relation between cigar smoking and alcohol consumption with respect to the risk of oropharyngeal cancers and cancers of the upper aerodigestive tract.

**Conclusions** Independently of other risk factors, regular cigar smoking can increase the risk of coronary heart disease, COPD, and cancers of the upper aerodigestive tract and lung. (N Engl J Med 1999;340:1773-80.)

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CIGAR sales in the United States increased nearly 50 percent between 1993 and 1997. Over the same period, sales of large, "premium" cigars increased by 68 percent,<sup>1</sup> reversing a 20-year decline in cigar consumption that began in the early 1970s. The upward trend is mainly the result of increases in occasional cigar smoking by young and middle-aged men of relatively high socioeconomic status.<sup>1,2</sup> However, cigar smoking is also increasing among teenagers<sup>3</sup> and women.<sup>2</sup>

This resurgence of cigar smoking can be attributed to two factors. First, despite the established associations between cigar smoking and cancers of the upper aerodigestive tract<sup>4-7</sup> and lung<sup>8,9</sup> and chronic obstructive pulmonary disease (COPD),<sup>10,11</sup> cigars are generally perceived as safer than cigarettes. Second, cigars are heavily advertised and actively glamorized in the mass media.<sup>2</sup>

In contrast to the information on cigarette smoking, few data are available on the relation between cigar smoking and cardiovascular disease. To understand further the health risks associated with cigar smoking, we examined the association between cigar smoking (with no concomitant or past cigarette smoking or concomitant pipe smoking) and the incidence of coronary heart disease, ischemic stroke, hemorrhagic stroke, peripheral arterial disease, COPD and related conditions, and cancer at selected sites in a large cohort of men who were members of a health maintenance organization.

### METHODS

#### Study Cohort

The study cohort was composed of 17,774 men 30 to 85 years of age who were enrolled in the Kaiser Permanente Medical Care

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Program of Northern California, who reported never having smoked cigarettes, and who were not currently pipe smokers. The Kaiser Permanente health plan offers comprehensive, prepaid medical care to more than one quarter of the population in the geographic areas served. The ethnic background and socioeconomic status of Kaiser Permanente members are representative of the local population, except that the extremes of wealth and poverty are underrepresented.<sup>12</sup>

The cohort was a subgroup of a larger population of 207,165 members (112,638 females and 94,527 males) 14 years of age or older who underwent multiphasic health checkups (voluntary health examinations at the time of enrollment) in San Francisco and Oakland, California, from 1964 through 1973.<sup>13</sup> If a study participant had more than one checkup, only the data from the first were used. Women were not included because only 25 reported smoking cigars but not cigarettes or a pipe.

Information on lifestyle and physiologic characteristics was collected according to standard procedures.<sup>14,15</sup> Serum cholesterol was measured with an AutoAnalyzer (Technicon, White Plains, N.Y.) from 1964 through 1968, with an Autochemist (AGA, Stockholm, Sweden) from 1969 through 1972, and with an AutoAnalyzer (model SMA-12, Technicon) in 1973. Self-reported alcohol consumption during the previous year was categorized as follows: no alcoholic drinks, one or two drinks per day, three to five drinks per day, and six or more drinks per day. The presence of diabetes mellitus, cardiovascular disease, and COPD was determined on the basis of the patients' reports. Of the 17,774 participating men, 485 reported a history of cardiovascular disease only, 657 reported a history of COPD only, 53 reported a history of both cardiovascular disease and COPD, and 16,579 reported neither.

Data on the subsequent incidence of cancer were gathered from Kaiser Permanente hospitalization records and local tumor registries. From 1969 through 1971, the Third National Cancer Survey provided information on registry-verified cases among residents of the five counties of the San Francisco Bay area; starting in 1973, this information was supplied by the local Surveillance, Epidemiology, and End Results program. Case reporting in 1972 was incomplete as cancer registries prepared for the initiation of that program. In 1988, inclusion in this tumor registry was extended to members living in outlying counties and to hospitalized patients in the Sacramento and Stockton areas. Starting in 1990, all Kaiser Permanente subscribers in northern California were included in the tumor registry. We studied cancers of the oropharynx, the upper aerodigestive tract (the oropharynx plus the nose, larynx, and esophagus), the lung, the pancreas, the kidney, the bladder, and the colon and rectum, all smoking-related cancers (at all the sites just listed, considered together), and all cancers except nonmelanoma skin cancer, considered together. We studied colorectal cancer because it is common and because some studies have shown cigarette smoking to be related to the risk of cancer and of polyps in the large bowel.<sup>16,17</sup>

The incidence of nonfatal or fatal cardiovascular disease and of COPD and related conditions was determined on the basis of information from an automated data base of hospital-discharge diagnoses beginning on January 1, 1971. These diseases, classified according to the *International Classification of Diseases, Eighth Revision* (ICD-8) and *Ninth Revision* (ICD-9), were as follows: coronary heart disease, ICD-8 and ICD-9 codes 410 through 414; ischemic stroke, ICD-8 codes 432 through 438 and ICD-9 codes 433 through 438; hemorrhagic stroke, ICD-8 codes 430 and 431 and ICD-9 codes 430 through 432; peripheral arterial disease, ICD-8 and ICD-9 codes 440 through 448; and COPD and related conditions, ICD-8 and ICD-9 codes 490 through 496. If a study participant was hospitalized more than once, only data from the first hospitalization were selected. For cardiovascular outcomes, results when we considered the primary diagnosis were similar to those when we considered any diagnosis (i.e., primary or secondary); therefore, only the results based on the primary diagnosis are shown. Because there were only 12 cigar smokers with primary discharge diagnoses of COPD, we present results for COPD as either a primary diagnosis or as a secondary diagnosis.

In a recent study,<sup>18</sup> the automated data base of hospital-discharge files was shown to provide information consistent with physicians' diagnostic impressions on chart review. Fatal outcomes through the end of 1995 were obtained with the use of Mortlink, an algorithm derived from the California Automated Mortality Linkage System.<sup>19</sup> The underlying causes of death were categorized according to the ICD-8 and ICD-9 codes.<sup>20,21</sup> Data on mortality were available regardless of continuing membership in the health plan, and out-of-state mortality was estimated to be less than 2 percent.<sup>19</sup>

For the analysis of the incidence of cancer, follow-up for each man ended when the cancer under consideration developed, when he died or left the health plan for any reason, or on December 31, 1996, whichever came first. For the analyses of cardiovascular disease and of COPD, person-time was calculated as the number of years elapsed between base line (January 1, 1971) and hospitalization, death, the end of the study (December 31, 1995), or termination of membership in the health plan. Participants were considered to have left the health plan if their names did not appear in the midyear membership roster for two consecutive years (even if the participant later rejoined the plan); data were censored as of December 31 of the year before the lapse in membership began. We set this criterion because we did not consider out-of-plan hospitalizations in our analyses. About 40 percent of study participants were followed until the end of the study. The rate of attrition due to a change in insurance coverage or death was approximately 3 percent per year, and the median follow-up time was 18 years (range, 1 to 25).

#### Determination of Cigar-Smoking Status and Dose

A self-administered questionnaire was used to identify, from among the initial population of health-plan enrollees, 17,774 men who reported never having smoked cigarettes and who were not currently smoking a pipe. Of these, 1546 (8.7 percent) reported currently smoking cigars, and 16,228 (91.3 percent) reported not currently smoking cigars. Cigar smokers were further classified according to whether they smoked fewer than 5 cigars per day, 5 to 10 cigars per day, or more than 10 cigars per day. The questionnaire did not inquire about the degree of inhalation, the length of time cigars had been smoked, or the type of cigar usually smoked. Because cigar and pipe smoking in the past (i.e., before one year earlier) was not ascertained, both the cigar-smoking and the non-cigar-smoking groups may have included some former cigar and pipe smokers.

#### Statistical Analysis

Age-adjusted rates (per 10,000 person-years) of study outcomes, according to cigar-smoking status, were estimated by Poisson regression analysis. Age-adjusted relative risks associated with cigar smoking (as compared with no cigar smoking) were calculated with the use of Cox proportional-hazards models.<sup>22</sup> Covariates included in multivariate analyses of the incidence of cancer and COPD were the following: age, race (Asian, black, or other or unknown, as compared with white), body-mass index, history of diabetes mellitus, current alcohol consumption (fewer than three, three to five, or six or more drinks per day or an unknown amount, as compared with no alcohol consumption), and any recent or past occupational exposure, as compared with no exposure (to hazardous chemicals, cleaning fluids, or solvents; insect or plant sprays; ammonia, chlorine, ozone, or nitrous gases; engine-exhaust fumes for more than two hours per day; plastics or resin fumes; lead or other metal fumes; asbestos or grain dusts; silica or rock dust or dust from sandblasting or grinding; or x-rays or radioactivity).

In multivariate analyses of cardiovascular outcomes, we included (in addition to the covariates listed above, and with the exception of occupational exposure) educational attainment (no college education as compared with at least some college education), systolic blood pressure, and total serum cholesterol level. To prevent the loss of data, the last two variables were entered as indicators representing quartiles (with the lowest quartile as the reference group) and a dummy variable that modeled missing values

**TABLE 1.** BASE-LINE CHARACTERISTICS OF 17,774 MEN, 30 TO 85 YEARS OF AGE, WHO REPORTED NEVER HAVING SMOKED CIGARETTES AND WHO WERE NOT CURRENTLY SMOKING A PIPE, ACCORDING TO CIGAR-SMOKING STATUS.\*

VARIABLE	NO CIGAR SMOKING (N=16,228)	CIGAR SMOKING (N=1546)
Age (yr)	46.1±12.0	47.8±11.7
Body-mass index†	25.9±3.4	26.9±3.7
Systolic blood pressure (mm Hg)	136±20	138±21
Diastolic blood pressure (mm Hg)	79±14	81±14
Serum total cholesterol (mg/dl)‡	227±42	229±42
	no. (%)	
Level of education		
No college	6,248 (39)	710 (46)
At least some college	7,448 (46)	634 (41)
Unknown	2,532 (16)	202 (13)
Race		
Asian	1,218 (8)	38 (2)
Black	1,889 (12)	229 (15)
Other or unknown	1,002 (6)	51 (3)
White	12,119 (75)	1228 (79)
Alcohol (no. of drinks/day)		
0	4,699 (29)	138 (9)
1-2	9,049 (56)	1005 (65)
3-5	1,044 (6)	207 (13)
≥6	281 (2)	77 (5)
Unknown	1,155 (7)	119 (8)
Diabetes mellitus	491 (3)	73 (5)
Any occupational hazard	5,799 (36)	523 (34)

\*Plus-minus values are means ±SD. Because of rounding, not all percentages total 100.

†The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡To convert values for cholesterol to millimoles per liter, multiply by 0.02586.

(altogether, these variables were missing for fewer than 5 percent of the subjects).

In the analysis of cardiovascular outcomes, men who had cardiovascular disease at base line, but not those who had COPD at base line, were excluded. Likewise, in the analysis of COPD, men who had COPD at base line, but not those with cardiovascular disease at base line, were excluded, and men with cancer at base line were excluded from the analysis of cancer at that site. To assess potential misclassification of exposure, we ascertained the continuation of cigar smoking and any switching to or addition of cigarette smoking during follow-up.

## RESULTS

Of the 1546 cigar smokers, 1177 (76 percent) smoked fewer than five cigars per day, and 263 (17 percent) smoked five or more per day. In 106 (7 percent), the number of cigars smoked per day was unknown. In contrast to men who did not smoke cigars, cigar smokers were, on average, slightly older; had a higher body-mass index, higher systolic and diastolic blood pressures, and a higher serum level of

total cholesterol; and were more likely to have diabetes mellitus (Table 1). In addition, cigar smokers were more likely to be black or white and less likely to be Asian, to have no college education, and to consume one or two, three to five, or six or more alcoholic drinks per day.

The total number of person-years of follow-up was 228,512 for men who did not smoke cigars and 20,176 for those who did. The age-adjusted rates of occurrence per 10,000 person-years for all cardiovascular outcomes and for COPD and related conditions were consistently higher among cigar smokers than among nonsmokers (Table 2). In multivariate analyses, cigar smokers were at moderately higher risk for coronary heart disease and COPD (Table 2). On the other hand, no significant associations were found between cigar smoking and ischemic stroke, hemorrhagic stroke, or peripheral arterial disease.

In multivariate analyses of the incidence of cancer, cigar smokers had approximately twice as high a risk of cancer of the oropharynx, upper aerodigestive tract, or lung as nonsmokers, and about one and a half times as high a risk of all smoking-related cancers considered together. The incidence of the other individual cancers studied and of all cancers combined was not substantially greater in cigar smokers; the lower bounds of the 95 percent confidence limits for the relative risks of these cancers were below 1.0 (Table 3). Except for all cancers combined, there were clear dose-response relations: the risks associated with cigar smoking were greater among those who smoked five or more cigars a day, as compared with those who smoked fewer (Table 4). There was also a significantly increased risk of peripheral arterial disease among smokers of five or more cigars per day (Table 4). Dose-response data are not presented for hemorrhagic stroke because there were no hemorrhagic events among smokers of five or more cigars per day.

With respect to oropharyngeal cancer, there appeared to be synergism between cigar smoking and alcohol consumption, although the number of cases examined was very small. When cigar smokers were divided into a group that reported consuming two or fewer alcoholic drinks per day and a group that reported consuming three or more drinks per day, and nonsmokers who consumed two or fewer drinks per day were considered the reference group, the number of cases of oropharyngeal cancer and the relative risks were as follows: three or more drinks and no smoking, one case and a relative risk of 0.38 (95 percent confidence interval, 0.05 to 2.83); two or fewer drinks and cigar smoking, four cases and a relative risk of 1.50 (95 percent confidence interval, 0.53 to 4.25); and three or more drinks and cigar smoking, four cases and a relative risk of 7.56 (95 percent confidence interval, 2.65 to 21.60). The findings were similar for upper aerodigestive tract

**TABLE 2.** INCIDENCE AND RISK OF CARDIOVASCULAR DISEASES AND COPD IN RELATION TO CIGAR SMOKING AMONG 17,774 MEN.\*

OUTCOME†	NO CIGAR SMOKING (N=16,228)	CIGAR SMOKING (N=1546)	P VALUE
Coronary heart disease			
No. of events	2222	244	
Age-adjusted rate per 10,000 person-years	78.5	99.4	
Multivariate-adjusted relative risk (95% CI)	1.00	1.27 (1.12–1.45)	<0.001
Ischemic stroke			
No. of events	808	82	
Age-adjusted rate per 10,000 person-years	20.9	21.9	
Multivariate-adjusted relative risk (95% CI)	1.00	1.07 (0.85–1.34)	0.55
Hemorrhagic stroke			
No. of events	162	16	
Age-adjusted rate per 10,000 person-years	5.3	5.6	
Multivariate-adjusted relative risk (95% CI)	1.00	1.12 (0.67–1.90)	0.65
Peripheral arterial disease			
No. of events	212	24	
Age-adjusted rate per 10,000 person-years	7.1	8.9	
Multivariate-adjusted relative risk (95% CI)	1.00	1.29 (0.84–1.98)	0.23
COPD and related conditions			
No. of events	446	57	
Age-adjusted rate per 10,000 person-years	14.9	21.1	
Multivariate-adjusted relative risk (95% CI)	1.00	1.45 (1.10–1.91)	0.008

\*CI denotes confidence interval. The age-adjusted rate was the calculated rate at a median age of 45 years in both cigar smokers and nonsmokers. Adjustment factors for the calculation of multivariate-adjusted risks are given in the Methods section.

†An outcome of coronary heart disease, ischemic stroke, hemorrhagic stroke, or peripheral arterial disease was a principal diagnosis at hospital discharge or death due to that illness. An outcome of COPD or a related condition was a principal or secondary diagnosis at hospital discharge or death due to that illness.

cancers, of which 8 of 10 cases were oropharyngeal: among men who consumed three or more drinks per day and smoked cigars, the relative risk of one such cancer was 6.24 (95 percent confidence interval, 2.47 to 15.77).

Of the 1546 cigar smokers, 438 (28 percent) returned for an additional checkup four years after base line, and 171 (11 percent) returned eight years after base line. Among those who returned at four years, 281 (64 percent) reported continued cigar smoking, and among those who returned at eight years, 86 (50 percent) reported continued cigar smoking. Very few of the cigar smokers who returned for follow-up had changed to or added cigarette smoking: 19 (4 percent) had done so four years after base line, and 4 (2 percent) had done so eight years after base line.

## DISCUSSION

In this cohort study of male health-plan enrollees, cigar smoking was associated with a moderate but significant increase in the risk of coronary heart disease, COPD and related conditions, and cancers of the lung and the upper aerodigestive tract. All these outcomes showed dose–response relations in that the increased risks were mainly seen among men who smoked five or more cigars per day, as compared with those who did not smoke. No significant

associations were found between cigar smoking and ischemic or hemorrhagic stroke or cancer of the pancreas, kidney, bladder, or colorectum. By comparison, whereas the relative risks of disease associated with cigar smoking were moderate (most were less than 2), typical relative risks associated with current cigarette smoking by men are 1.5 to 3.0 for coronary heart disease, 9 to 25 for COPD, 8 to 24 for lung cancer, and 4 to 12 for oropharyngeal cancer.<sup>2,23,24</sup> Because about half of the cigar smokers who were evaluated eight years after base line reported having quit smoking cigars, it is likely that the effects of continued cigar smoking were underestimated. Another possible source of bias toward the null hypothesis is our inability to account for the exposure of people who never smoked to environmental tobacco smoke.

Among studies of cigar smoking and heart disease, conclusions have been mixed. In an American Cancer Society study in nine states, the age-adjusted mortality ratio for coronary heart disease among cigar smokers as compared with nonsmokers was 1.28.<sup>25</sup> A study of a cohort of U.S. veterans found that mortality due to coronary heart disease was higher among smokers of only cigars than among nonsmokers (standardized mortality ratio, 1.12), as was mortality due to cardiovascular disease (stand-

**TABLE 3.** INCIDENCE AND RISK OF CANCER AT SELECTED SITES IN RELATION TO CIGAR SMOKING AMONG 17,774 MEN.\*

OUTCOME†	NO CIGAR SMOKING (N=16,228)	CIGAR SMOKING (N=1546)	P VALUE
Cancer of the oropharynx			
No. of events	39	8	
Age-adjusted rate per 10,000 person-years	0.9	2.0	
Multivariate-adjusted relative risk (95% CI)	1.00	2.61 (1.18–5.76)	0.02
Cancers of the upper aerodigestive tract‡			
No. of events	57	10	
Age-adjusted rate per 10,000 person-years	1.4	2.4	
Multivariate-adjusted relative risk (95% CI)	1.00	2.02 (1.01–4.06)	0.04
Lung cancer			
No. of events	54	11	
Age-adjusted rate per 10,000 person-years	1.4	3.0	
Multivariate-adjusted relative risk (95% CI)	1.00	2.14 (1.12–4.11)	0.02
Pancreatic cancer			
No. of events	46	6	
Age-adjusted rate per 10,000 person-years	1.2	1.6	
Multivariate-adjusted relative risk (95% CI)	1.00	1.21 (0.51–2.88)	0.66
Cancer of the kidney			
No. of events	50	5	
Age-adjusted rate per 10,000 person-years	1.4	1.4	
Multivariate-adjusted relative risk (95% CI)	1.00	1.08 (0.43–2.71)	0.87
Bladder cancer			
No. of events	99	10	
Age-adjusted rate per 10,000 person-years	2.6	2.7	
Multivariate-adjusted relative risk (95% CI)	1.00	1.05 (0.55–2.01)	0.89
All smoking-related cancers§			
No. of events	297	41	
Age-adjusted rate per 10,000 person-years	7.8	11.1	
Multivariate-adjusted relative risk (95% CI)	1.00	1.42 (1.02–1.98)	0.04
Colorectal cancer			
No. of events	332	39	
Age-adjusted rate per 10,000 person-years	8.8	11.1	
Multivariate-adjusted relative risk (95% CI)	1.00	1.12 (0.80–1.57)	0.51
All cancers (except nonmelanoma skin cancer)			
No. of events	1,806	201	
Age-adjusted rate per 10,000 person-years	52.7	60.3	
Multivariate-adjusted relative risk (95% CI)	1.00	1.07 (0.93–1.25)	0.35

\*CI denotes confidence interval.

†The age-adjusted rate was the calculated rate at a median age of 45 years in both cigar smokers and nonsmokers. Adjustment factors for the calculation of multivariate-adjusted risks are given in the Methods section.

‡Cancers of the upper aerodigestive tract comprised cancers of the oropharynx, nose, larynx, and esophagus.

§Smoking-related cancers comprised cancers of the upper aerodigestive tract, lung, pancreas, kidney, and bladder.

ardized mortality ratio, 1.10).<sup>6</sup> A study in the north-eastern United States found no association between cigar smoking and coronary events among 572 men who had had a first nonfatal myocardial infarction and 934 hospitalized control subjects.<sup>26</sup> A Danish study found a significant association between the smoking of cheroots (small, open-ended cigars) and the risk of myocardial infarction, but the sample included former cigarette smokers, who were more likely than others to inhale the smoke.<sup>27</sup> In a cohort of 634 men younger than 60 years of age, cigar and pipe smoking had an adverse effect on four-year survival after a first attack of unstable angina or a first myocardial infarction.<sup>28</sup> Cigar or pipe smoking was

a predictor of death due to aortic aneurysm among middle-aged civil servants in the United Kingdom.<sup>29</sup> The American Cancer Society's Cancer Prevention Study I revealed that rates of death due to coronary heart disease increased with an increasing number of cigars smoked each day and among cigar smokers who inhaled the smoke moderately or deeply.<sup>2</sup> The lack of association between the smoking of cigars only and cerebrovascular disease in our study is consistent with the data from the Cancer Prevention Study I.<sup>2</sup> In the Copenhagen City Heart Study, the relative risk of death due to COPD among persons who smoked cigars or cheroots was 10 for women and 3.7 for men.<sup>11</sup> In the Cancer Prevention Study I,

**TABLE 4.** MULTIVARIATE-ADJUSTED RISK OF CARDIOVASCULAR DISEASES, COPD, AND CANCER IN RELATION TO THE AMOUNT OF CIGAR SMOKING AMONG 17,774 MEN.\*

OUTCOME	<5 CIGARS PER DAY (N=1177)			≥5 CIGARS PER DAY (N=263)		
	NO. OF EVENTS	RELATIVE RISK (95% CI)	P VALUE	NO. OF EVENTS	RELATIVE RISK (95% CI)	P VALUE
Coronary heart disease	182	1.20 (1.03–1.40)	0.02	62	1.56 (1.21–2.01)	<0.001
Ischemic stroke	58	1.02 (0.78–1.34)	0.88	24	1.29 (0.85–1.94)	0.23
Peripheral arterial disease	15	1.09 (0.64–1.86)	0.73	9	2.17 (1.09–4.32)	0.02
COPD and related conditions	39	1.30 (0.93–1.81)	0.12	18	2.25 (1.39–3.65)	0.001
Oropharyngeal cancer	3	1.34 (0.41–4.42)	0.63	4	7.20 (2.44–21.2)	<0.001
Cancers of the upper aerodigestive tract†	4	1.12 (0.40–3.12)	0.84	5	5.20 (2.00–13.5)	<0.001
Lung cancer	6	1.57 (0.67–3.66)	0.30	3	3.24 (1.01–10.4)	0.04
All smoking-related cancers‡	25	1.17 (0.77–1.77)	0.46	12	2.26 (1.26–4.07)	0.01
All cancers (except non-melanoma skin cancer)	155	1.11 (0.94–1.31)	0.22	33	0.98 (0.69–1.38)	0.89

\*Adjustment factors for the calculation of multivariate risks are given in the Methods section. The reference group is men who did not smoke cigars (n=16,228). In 106 men, the amount of cigar smoking was unknown. CI denotes confidence interval.

†Cancers of the upper aerodigestive tract comprised cancers of the oropharynx, nose, larynx, and esophagus.

‡Smoking-related cancers comprised cancers of the upper aerodigestive tract, lung, pancreas, kidney, and bladder.

the degree of inhalation showed a highly significant relation to mortality associated with COPD.<sup>2</sup>

That cigar smoking causes cancer in the oropharynx and the upper aerodigestive tract, including the larynx and esophagus, is well established.<sup>4-7</sup> The increase in the risk of these diseases associated with cigar smoking has been reported to be similar to that associated with cigarette smoking,<sup>2</sup> a point that could not be confirmed in our study, which excluded cigarette smokers. For cancers at these sites, we found that relative risks tended to be lower than those others have reported,<sup>2,4-7</sup> but this discrepancy may be due to differences in study design.

We observed an apparent synergism between cigar smoking and high levels of alcohol consumption in relation to the risk of cancers of the oropharynx and upper aerodigestive tract, as has been reported for cigarette smoking and alcohol use.<sup>5,28</sup> The possibility of a synergistic relation must be viewed with caution, however, because of the small number of cases in patients who combined cigar use and alcohol consumption and because of the open-ended nature of the category of high alcohol consumption ( $\geq 3$  drinks per day) combined with cigar smoking.<sup>30</sup> It has been suggested, but not proved, that alcohol might enhance the carcinogenicity of tobacco smoke in the upper aerodigestive tract by dissolving carcinogens in the smoke or by increasing the susceptibility of the mucosa to carcinogens, possibly as a result of nutritional deficiencies associated with heavy alcohol consumption.<sup>5</sup>

As noted elsewhere,<sup>2,31,32</sup> the associations between cigar smoking and COPD and lung cancer were

weaker than those seen for cigarette smoking, probably because cigar smoke is usually not inhaled deeply. Inhalation was not assessed in the men in our study, but in a smaller group of men examined between 1979 and 1985, about 10 percent of 225 cigar smokers reported that they inhaled.<sup>33</sup> We also did not assess duration of cigar smoking or the type of cigar consumed. However, in the same subgroup of men, 70 percent had smoked for at least 10 years, and 21 percent smoked large cigars.<sup>33</sup> In addition, we were unable to separate occasional cigar smokers (those who smoked a few cigars each month) or sporadic cigar smokers (those who smoked a few cigars each year) from others in the study group. Thus, our findings should not be generalized to people who smoke cigars infrequently. We also cannot rule out residual confounding or effect modification by other factors, such as genetic traits, or lifestyle characteristics that were not measured in the study, such as diet and physical activity. However, in our analyses, we controlled for body-mass index, systolic blood pressure, and serum total cholesterol level, which are important variables mediating the effect of diet and physical activity on the risk of cardiovascular disease.

The strengths of our study include the large sample, the long duration of follow-up, the availability of data on several risk factors (which allowed us to perform multivariate adjustment), and the low likelihood of ascertainment bias. Participants in this health plan, such as the men in this study, have equal access to medical care, regardless of their socioeconomic and health status.

It is well documented that cigar smoke contains the same toxic and carcinogenic compounds that are found in cigarette smoke<sup>34,36</sup> and that persons who smoke four or more cigars per day are exposed to an increased amount of smoke, equivalent to the smoke of 10 cigarettes per day.<sup>32</sup> The mainstream smoke from cigars (the smoke drawn into the mouth from the butt end) contains greater concentrations of nicotine, benzene, polynuclear aromatic hydrocarbons (including benzo[*a*]pyrene), hydrogen cyanide, lead nitrogen oxides, *N*-nitrosamines, ammonia, and carbon monoxide than does the mainstream smoke from cigarettes.<sup>35,36</sup> As a result, persons who inhale cigar smoke have markedly increased concentrations of carboxyhemoglobin.<sup>37</sup> Furthermore, the alkaline pH of cigar smoke facilitates the absorption of nicotine through the buccal and nasal mucosae.<sup>38,39</sup> Another potential reason why cigar smoking may increase the risk of coronary heart disease is the associated high levels of exposure to environmental tobacco smoke. Even cigar smokers who do not inhale are exposed to their own environmental tobacco smoke, a clearly documented risk factor for coronary heart disease<sup>40-44</sup> and COPD.<sup>45-47</sup>

In summary, our data confirm that cigar smoking is related to a moderate increase in the risk of COPD and cancers of the upper aerodigestive tract and lung, and they add new evidence that cigar smoking is associated with a moderate but significant increase in the risk of coronary heart disease. The resurgence of cigar smoking in recent years is a matter of substantial concern.

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