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Research Article

Cancer Prevention Research

Association between Cigar or Pipe Smoking and Cancer Risk in Men: A Pooled Analysis of Five Cohort Studies

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Abstract

Introduction: Use of non-cigarette tobacco products such as cigars and pipe has been increasing, even though these products entail exposure to similar carcinogens to those in cigarettes. More research is needed to explore the risk of these products to guide cancer prevention efforts.

Methods: To measure the association between cigars and/or pipe smoking, and cancer incidence in men, we performed meta-analyses of data from five prospective cohorts. Cox regression was used to evaluate the association between different aspects of cigars and pipe smoking and risk of each smoking-related cancer (head and neck, esophagus, lung, stomach, liver, pancreas, kidney, and bladder) for each study. Adjusted HRs were combined using random-effects models.

Results: Cigars and/or pipe smokers were at increased risk for head and neck [HR, 1.51; 95% confidence interval (CI), 1.22–1.87], lung (HR, 2.04; 95% CI, 1.68–2.47), and liver cancers (HR, 1.56; 95% CI, 1.08–2.26). Ever-smokers of cigars and/or pipe had an increased risk of developing a smoking-related cancer when compared with never smokers of any tobacco product (overall HR, 1.07; 95% CI, 1.03–1.12). The risk for smoking-related cancers was also increased in mixed smokers who smoked cigars or pipe as well as cigarettes, even when they were smoking predominantly pipe or cigars.

Discussion: This pooled analysis highlights the increased risk for smoking-related cancers, particularly for lung and head and neck cancers in exclusive and predominant smokers (former and current) of cigars and pipe. Tobacco prevention efforts should include these products in addition to cigarettes. *Cancer Prev Res; 10(12); 704–9. ©2017 AACR.*

Introduction

Tobacco smoking represents the leading single preventable cause of chronic disease, including cancer, cardiovascular, and respiratory diseases (1). During the past few decades, the prevalence of cigarette smoking, the most common type of tobacco use, has decreased in the United States and several other high-income countries (2). In contrast, recent reports have shown an increase in the use of other tobacco products such as cigars and cigarillos in the United States and many other areas of the world (3, 4). The U.S. Centers for Disease Control and Prevention (CDC) have reported that from 2000 to 2015, although total population cigarette consumption declined by 39%, large cigar and pipe consumption increased by 179.6% and 556.4%, respectively (5). Among the suggested reasons for this increase in use are the relatively lower cost of these other tobacco products, as they are usually exempted (at least partially) from cigarette-specific taxes and the belief that these products are less harmful than cigarettes. Cigar smoking is an emerging public health hazard, especially in youth. U.S. data from the 2011–2015 National Youth Tobacco Surveys reported that in 2015, about 1.4 million middle and high school students used cigars (6).

The smoke from cigars and pipe tobacco contains many harmful and potentially harmful compounds found in cigarette smoke, and using these products may expose smokers to these compounds at higher levels per puff than cigarettes (7, 8). For example, cigar and pipe smoke may contain levels of carcinogens such as benzo[a]pyrene that are equivalent or, in some instances, higher than those in cigarette smoke (9). Rickert and colleagues reported that total particulate matter extracts from cigars and cigarillos were up to 200% more mutagenic, and for pipe 44% more mutagenic per unit of nicotine, relative to cigarette smoke (7). However, the majority of prospective studies that have investigated the association between cigarette smoking and cancer have not investigated associations for other tobacco-smoking products. In published studies, the number of participants using those products was typically too small for the results to be reported separately and could not provide clear conclusions on the association of those products and cancer risk. Because of the long latency of health

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effects of tobacco products, the full range of effects of current patterns of increased use of cigar and pipe smoking in the young as well as in other population groups may not become apparent for years. As the evidence from prospective studies regarding the health effects of smoking tobacco products other than cigarettes is limited, more research is needed to explore the cancer risk from these products to guide cancer prevention efforts.

In this analysis, we assessed the association between smoking cigars and pipe, and cancer risk for men using pooled data from prospective epidemiologic studies. Cigar and pipe smoking was too uncommon in women to study in these cohorts. Our main aim was to better characterize and provide precise estimates of the relative risk of smoking-related cancers associated with cigar and pipe smoking.

Materials and Methods

We performed meta-analyses of data from five prospective cohort studies (listed in Table 1) that are part of the US National Cancer Institute (NCI) Cohort Consortium and that had collected data on cigar and pipe smoking. The NCI Cohort Consortium is an extramural–intramural partnership coordinated by the NCI to address the need for large-scale collaborations to pool the large quantity of data necessary to conduct a wide range of cancer studies. Only men were included in our analysis as these products were uncommon in women. We also excluded participants with a history at baseline of any cancer. The five studies included were the Netherlands Cohort Study (NLCS; ref. 10), the Melbourne Collaborative Cohort Study (MCCS; ref. 11), the VITamins And Lifestyle (VITAL) cohort (12), the NIH-AARP Diet and Health study, (13) and the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO; ref. 14). All data from the participating studies were received in deidentified form at the Icahn School of Medicine at Mount Sinai in New York. Harmonized variables were developed based on a detailed review of the original information used in each cohort.

Exposure variables

For the main analysis, variables on smoking status (ever smoking of cigars, pipe, or cigarettes only or in combination) were derived for each study. Never smokers were the referent category, and a subject was considered to be never smoker if he responded "no" to ever smoking cigarettes, cigars, or pipe. Subjects were considered to be ever pipe smoker or ever cigar smoker if he responded "yes" to ever smoking that product (but responded "no" to ever smoking cigarettes). Thus, our primary analysis was restricted to subjects who were had never smoked cigarettes. Because many ever-smokers of pipe or cigars have also smoked cigarettes, we also performed additional analysis in mixed smokers by modeling exclusive and predominant lifetime consumption of individual smoking products. The latter variables could only be computed from two studies (VITAL and NLCS) that had the required detailed exposure information on pipe and cigar use. To do this, we calculated product-specific lifetime consumption (in grams of tobacco) on the basis of International Agency for Research on Cancer estimates of average unit weights (9, 15) as follows: frequency of cigarette smoking (number of cigarettes per day) $\times$ duration of cigarette smoking (years) $\times$ 1 (assuming a cigarette contains 1 g of tobacco on average); frequency of cigar smoking (number of cigars per day) $\times$ duration of cigar smoking (years) $\times$ 4 (assuming a cigar contains 4 g of tobacco on average); and frequency of pipe smoking (number of pipe fills per day) $\times$ duration of pipe smoking (years) $\times$ 3.5 (assuming a pipe fill contains 3.5 g of tobacco on average). Total lifetime consumption of smoking tobacco equaled the sum of product-specific lifetime consumptions for cigarettes, cigars, and pipe. Product-specific lifetime consumptions of cigarettes, cigars, and pipe were then divided by the total lifetime consumption of all three smoking products combined. Exclusive smoking behaviors for each product were defined as 100% lifetime consumption of that one product. Predominant smoking behaviors for each product were defined as 66.6% to 99.9% of lifetime consumption of that one product. The reference group for exclusive/predominant smokers

Table 1. Characteristics of male participants by study at time of enrollment

	NLCS (n = 58,279)[a]	MCCS (n = 16,491)	VITAL (n = 37,372)	NIH-AARP (n = 339,666)	PLCO (n = 72,632)
Country	Netherlands	Australia	USA	USA	USA
Enrollment years	1986	1990–1994	2000–2002	1995–1996	1993–2001
Median duration of follow-up, years	17.3	18.6	9.9	15.5	12.5
Age at enrollment, years (mean $\pm$ SD)	61.3 $\pm$ 4.2	55.6 $\pm$ 8.8	62.0 $\pm$ 7.4	62.3 $\pm$ 5.3	62.7 $\pm$ 5.3
BMI categories in kg/m^2 (%)					
<18.5	0.5	0.2	0.7	0.4	0.3
18.5 to 25	52.8	27.4	28.3	23.7	25.6
25 to 30	42.9	53.2	48.2	46.2	49.5
$\geq$30	3.8	19.1	22.8	29.8	24.5
Ethnicity, white (%)	100.0	100.0	92.0	92.5	88.3
Smoking status, n (%)					
Never smoker	201 (9.2)	6,592 (40.0)	12,434 (33.3)	77,664 (22.9)	20,854 (28.7)
Ever cigarette smokers only	1,322 (60.3)	7,398 (44.9)	13,283 (35.5)	150,975 (44.5)	25,179 (34.7)
Ever cigar smokers only	46 (2.1)	56 (0.3)	486 (1.3)	4,522 (1.3)	1,512 (2.1)
Ever pipe smokers only	8 (0.4)	95 (0.6)	990 (2.7)	5,214 (1.5)	1,431 (2.0)
Ever both cigarettes and cigars	283 (12.9)	461 (2.8)	1,805 (4.8)	14,767 (4.4)	4,469 (6.2)
Ever both cigarettes and pipe	90 (4.1)	1,044 (6.3)	4,181 (11.2)	27,700 (8.2)	6,999 (9.6)
Ever both pipe and cigars	23 (1.1)	31 (0.2)	776 (2.1)	7,674 (2.3)	2,629 (3.6)
Ever cigarettes, pipe, and cigars	218 (10.0)	814 (4.9)	3,417 (9.1)	32,312 (9.5)	9,559 (13.2)
Ever smoker of pipe and/or cigars only[b]	77 (3.5)	182 (1.1)	1,476 (6.0)	17,410 (5.1)	5,572 (7.7)

Abbreviation: BMI, body mass index.

[a]NLCS subcohort = 2,191 for reporting baseline characteristics.

[b]Group represents ever-smokers of either pipe, cigars, or both and, never smokers of cigarettes.

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was never smokers, who were those with lifetime consumption of less than 100 cigarette-equivalents.

Cancer variables

Cancer cases were categorized by tumor site according to the International Classification of Diseases for Oncology, Second Edition, or the International Classification of Diseases, Ninth or Tenth Edition (13, 15–17). Smoking-related cancers included in this analysis were cancers of the head and neck, esophagus, lung, stomach, liver, pancreas, kidney, bladder, and colorectal (18). Prostate cancer was also studied as cigarette smoking has been shown in a meta-analysis to be associated with disease-specific mortality, whereas evidence for an association with prostate cancer risk is inconsistent (19, 20).

Data analysis

Associations between smoking-related variables and the risk of cancer were assessed for each study using Cox regression (19) to estimate HRs. Person-time was calculated from date of recruitment to the earliest of cancer diagnosis, death, or loss to follow-up. All analyses were adjusted for age at enrollment, body mass index at enrollment (<18.5, 18.5 to 24.9, 25.0 to 29.9, ≥30), race/ethnicity (white, non-white), socioeconomic status (completed high school or equivalent), average alcohol drinks per day, and family history of the cancer under study. For of the analysis of lung cancer, additional adjustment was made for history of chronic lung disease. Similarly, for analyses of liver cancer, further adjustment was made for history of chronic liver disease. For each specific cancer, the analysis was independent of the incidence of other tobacco-related cancers. Study-specific HRs (calculated from multivariate analysis) were then combined using random-effects models. The heterogeneity of the combined HRs was evaluated with Cochran's Q test and the Higgins I-squared statistic, and the HRs were considered statistically heterogeneous if they displayed $P < 0.05$ and/or $I^2 > 50\%$ (21). All analyses were performed using STATA and SAS.

Results

Characteristics of participants from each participating study are presented in Table 1. The mean age at enrollment of subjects ranged from 55.6 years to 62.7 years and not statistically different between the five cohorts. The majority of participants in all studies were white. There was a significant variation between the studies in the patterns of smoking by geographical region. The NLCS (based in the Netherlands) had the lowest proportion of never smokers (of any tobacco product) at 9.2%, whereas 40% of the participants in the MCCS (based in Australia) were never smokers. Conversely, the MCCS had the lowest proportion (1.1%) of participants who reported ever smoking cigars and/or pipe (but not cigarettes) or a combination of both. For the three U.S. studies (VITAL, NIH-AARP, and PLCO), the proportion of participants ever smoking cigars and/or pipe ranged between 5.1% and 7.7%.

The combined adjusted HRs for cancer associated with ever-smoking cigars and/or pipe among those who did not smoke cigarettes are presented in Table 2. On calculating the combined HR for each smoking-related cancer independently, ever cigar and/or pipe smokers were at significantly increased risk for head and neck cancer [HR, 1.51; 95% confidence interval (CI), 1.22–1.87], lung cancer (HR, 2.04; 95% CI, 1.68–2.47), and liver cancer (HR, 1.56; 95% CI, 1.08–2.26). Other smoking-related cancers also showed trend toward increased risks with ever smoking of cigars and/or pipe with the HRs for all tobacco-related cancers greater than 1. Ever-smokers of cigars only, pipe only, or both had an increased risk of developing smoking-related cancers when compared with never smokers of any tobacco product (overall HR, 1.07; 95% CI, 1.03–1.12). These ever-smokers for cigars and/or pipe were also at increased risk for any cancer (smoking-related as well as nonsmoking-related) compared with never smokers (HR, 1.05; 95% CI, 1.02–1.08).

Table 2. HR for incidence of smoking-related cancers and all cancers in ever-smokers of pipe and/or cigars (but not cigarettes) relative to never smokers of any tobacco products

	Never smokers[a]	Ever cigar and/or pipe smokers	
Cancer group	**Cases**	**Cases**	**HR (95% CI)**
Smoking-related cancers[b]	5,257	1,299	1.07 (1.03–1.12)
Head and neck	386	131	1.51 (1.22–1.87)
Esophagus	166	54	1.29 (0.92–1.81)
Lung	365	198	2.04 (1.68–2.47)
Gastric	262	71	1.15 (0.86–1.53)
Pancreas	453	128	1.19 (0.91–1.57)
Liver	145	54	1.56 (1.08–2.26)
Kidney	667	168	1.13 (0.94–1.36)
Bladder	841	242	1.16 (0.98–1.37)
Colorectal	1,974	503	1.08 (0.97–1.20)
Prostate	4,896	1,037	0.93 (0.81–1.07)
All cancers[c]	20,478	5,007	1.05 (1.02–1.08)

NOTE: All analyses adjusted for age at enrollment, gender, body mass index at enrollment, race/ethnicity, socioeconomic status, average alcohol intake, and family history of specific cancer (and history of chronic lung disease for lung cancer analysis, history for chronic liver disease for liver cancer analysis).

[a]Never smokers—referent category.

[b]Smoking-related cancers include cancers of head and neck, esophagus, lung, stomach, pancreas, liver, kidney, bladder, and colorectal.

[c]All cancer incidence calculated for any invasive cancer including, smoking related-cancers.

Results stratified by type of product (ever cigar smokers only, ever pipe smokers only, ever-smokers of both) are presented in Table 3. The risk for a smoking-related cancer was increased in all three groups compared with never smokers of any tobacco product. Similarly, the risk for head and neck cancer, lung cancer as well as any cancer was increased in all three groups of smokers. Ever-smokers of both cigars and pipe showed an increased risk of gastrointestinal cancers, including liver (HR, 2.25; 95% CI, 1.46–3.46) as well as colorectal cancer (HR, 1.19; 95% CI, 1.02–1.39), suggesting a synergistic effect of these two products. Ever-smokers of pipe only showed an increased risk of bladder cancer (HR, 1.40; 95% CI, 1.07–1.84).

In our analysis of lifetime cumulative tobacco exposure (Table 4), we explored the association between each smoking-related cancer and smoking product category. Only NLCS and VITAL had detailed data about duration and frequency of use for each tobacco product. The risk of several cancers, including cancer of the esophagus, lung, kidney, and bladder, was increased in exclusive or predominant pipe smokers. The risk of head and neck cancer, lung cancer, gastric cancer, and kidney cancer as well as all cancers was increased in exclusive or predominant cigar smokers.

Discussion

We report an increased risk of smoking-related cancers with exclusive use of cigars or pipe when compared with never smokers of any tobacco products in a pooled analysis of data from five

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Table 3. HR for incidence of smoking-related cancers and total cancers in ever-smokers of pipe and/or cigars (but not cigarettes), by type of product(s) smoked

	Never smokers[a]	Ever cigar smokers only		Ever pipe smokers only		Ever cigar and pipe smokers only	
Cancer group	**Cases**	**Cases**	**HR (95% CI)**	**Cases**	**HR (95% CI)**	**Cases**	**HR (95% CI)**
Smoking-related cancers[b]	5,257	331	1.47 (1.34–1.61)	379	1.20 (1.07–1.33)	589	1.23 (1.13–1.34)
Head and neck	386	38	1.40 (0.98–2.00)	35	1.53 (1.07–2.20)	58	1.49 (1.09–2.03)
Esophageal	166	12	1.01 (0.56–1.84)	23	2.07 (1.28–3.34)	19	1.07 (0.65–1.76)
Lung	365	87	2.73 (2.06–3.60)	45	1.87 (1.33–2.64)	66	1.55 (1.13–2.11)
Gastric	262	27	1.06 (0.64–1.76)	16	1.07 (0.63–1.80)	28	1.18 (0.79–1.77)
Pancreas	453	34	1.10 (0.75–1.63)	16	1.21 (0.84–1.72)	60	1.19 (0.83–1.72)
Liver	145	10	0.76 (0.34–1.71)	12	1.32 (0.66–2.64)	32	2.25 (1.46–3.46)
Kidney	667	22	1.18 (0.88–1.58)	45	1.13 (0.83–1.54)	28	1.11 (0.85–1.46)
Bladder	841	63	1.14 (0.88–1.48)	73	1.40 (1.07–1.84)	106	1.15 (0.90–1.47)
Colorectal	1,974	139	0.96 (0.80–1.16)	130	1.08 (0.89–1.33)	234	1.19 (1.02–1.39)
Prostate	4,453	311	0.94 (0.79–1.11)	300	1.15 (0.86–1.53)	73	0.88 (0.70–1.10)
All cancers[c]	20,478	1,422	1.07 (1.02–1.16)	1,452	1.13 (1.08–1.18)	2,133	1.10 (1.06–1.15)

NOTE: All analyses adjusted for age at enrollment, gender, body mass index at enrollment, race/ethnicity, socioeconomic status, average alcohol intake, and family history of specific cancer (and history of chronic lung disease for lung cancer analysis, history for chronic liver disease for liver cancer analysis).

[a]Never smokers—referent category.

[b]Smoking-related cancers include cancers of head and neck, esophagus, lung, stomach, pancreas, liver, kidney, bladder, and colorectal.

[c]All cancer incidence calculated for any invasive cancer including, smoking-related cancers.

prospective cohorts. These findings suggest that both products independently contribute to cancer risk. Lung cancer showed the strongest association with smoking of both these products. An elevated risk was also observed for predominant cigar smokers and predominant pipe smokers compared with those of a reference group of never smokers of any product.

Our study is the largest pooled analyses using prospective cohort data to explore relationship between cancer incidence and exclusive cigar/pipe smoking. Our results are similar to previous reported analysis using data from a single study—European Prospective Investigation into Cancer Nutrition (EPIC) cohort. EPIC included 102,395 men from Europe and reported elevated risk for all smoking-related cancers combined in exclusive cigar smokers (HR, 1.3; 95% CI, 1.0–1.8), exclusive pipe smokers (HR, 1.7; 95% CI, 1.4–2.2), and exclusive cigarette smokers (HR, 2.2; 95% CI, 2.0–2.4). Similar to our results, this study also reported the strongest effects to be on lung cancer and upper aerodigestive tract cancers from exclusive cigar and pipe smoking (22). An increased risk for cancer-related mortality has also been reported from cigar and pipe smoking. In a systemic review of 22 studies using 16 prospective cohorts, current exclusive cigar smoking was associated with all cause-mortality as well as mortality from cancers of mouth, esophagus, lung, larynx as well as pancreas (23). The Cancer Prevention Study II enrolled 138,307 men in United States in 1982 and had 15,263 men who were exclusive current or former smokers of pipe. An analysis of prospective follow-up data showed that current pipe smoking, compared with never use of tobacco, was associated with an increased mortality from cancers of the lung, oropharynx, esophagus, colorectal, pancreas, and larynx. These risks were generally smaller than those associated with cigarette smoking and similar to or larger than those associated with cigar smoking (24, 25). A Swedish cohort study of 25,129 men reported similar risk of death from pipe or cigar smoking compared with cigarette smoking for most smoking-related causes of mortality (26).

Our study reported a stronger association for lung and head and neck cancers than for other cancers among exclusive cigar and/or pipe smoking. Our estimates for incident lung cancer were lower than those reported by a European case–control study in 5,621 male case patients with lung cancer and 7,255 male control subjects. This study reported an OR of 9.0 (95% CI, 5.8–14.1) for lung cancer with smoking cigars and cigarillos, but had only 43 exposed cases and 77 exposed controls in the analysis. The corresponding OR for exclusive smokers of pipe was reported to be 7.9 (95% CI, 5.3–11.8), based on 61 cases and 129 control subjects (27). In a pooled analysis of case–control studies from the International Head and Neck Cancer Epidemiology Consortium (comprising 13,935 cases and 18,691 controls in 19 studies from 1981 to 2007), the OR for head and neck cancer in exclusive cigar smokers and exclusive pipe smokers was 3.49 (95% CI, 2.58–4.73) and 3.71 (95% CI, 2.59–5.33), respectively, suggesting that cigar smoking and pipe smoking are independently associated with increased risk of head and neck cancers (15).

Consistent with previous studies, we found a significantly increased risk of cancer incidence in exclusive cigar and pipe smokers, and this is a matter of great public health concern given an increased use of these products in recent years. Even more concerning is the fact that a large proportion of those initiating use of these products are young adults. This may be due to reduced public awareness about the hazard from cigars and pipe as well as lack of large-scale prospective studies exploring the public health harms from these products. In 2014, the U.S. National Adult Tobacco Survey (2012–2013) found that the openness to use non-cigarette tobacco products among 5,985 young adults ages 18 to 29 years was 28.2% for hookah and 19.1% for cigars (28). In 2015, 1.6% of U.S. middle school students and 8.6% of high school students reported current use of cigars (either cigars, cigarillos, or little cigars; ref. 6). Therefore, there is an urgent need to study the health hazards from these products to help guide future cancer prevention efforts.

The major strength of our study was the evaluation of non-cigarette tobacco products by using a large pooled dataset from five international prospective cohorts. This overcame some of the problems with statistical power faced by individual established studies, given the historically low proportion of exclusive users of these products. Given the strong association between cigarette smoking and cancer incidence, we restricted analysis to exclusive smokers of cigars, pipe, or both to control for the confounding influence of cigarette smoking. Analysis of exclusive and predominant smokers of cigars and pipe was another key contribution. Although analysis of some of the cancers was limited by low

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Table 4. HR for each smoking-related cancer by exclusive/predominant smoking product categories

Cancer group		VITAL HR (95% CI)	NLCS HR (95% CI)	Combined HR (95% CI)
Head and neck	Predominantly cigar	-	2.41 (0.86–6.78)	-
	Exclusive cigar	3.56 (1.24–10.21)	1.83 (0.60–5.54)	2.59 (1.21–5.58)
	Predominantly pipe	0.82 (0.11–6.05)	3.51 (1.01–12.18)	2.34 (0.81–6.74)
	Exclusive pipe	0.86 (0.20–3.62)	7.17 (1.67–30.85)	2.47 (0.88–6.89)
Esophagus	Predominantly cigar	[a]	1.45 (0.37–5.73)	[b]
	Exclusive cigar	[a]	1.39 (0.35–5.47)	[b]
	Predominantly pipe	[a]	6.43 (1.90–21.73)	[b]
	Exclusive pipe	4.45 (1.39–14.21)	4.57 (0.72–28.98)	4.48 (1.68–11.99)
Lung	Predominantly cigar	-	9.51 (4.83–18.71)	-
	Exclusive cigar	1.64 (0.39–6.91)	8.61 (4.44–16.86)	6.44 (3.53–11.75)
	Predominantly pipe	2.17 (0.66–7.17)	15.29 (6.96–33.59)	8.46 (4.38–16.31)
	Exclusive pipe	1.25 (0.38–4.13)	8.76 (2.53–30.30)	3.18 (1.35–7.52)
Gastric	Predominantly cigar	[a]	1.79 (0.78–4.13)	[b]
	Exclusive cigar	2.51 (0.58–10.88)	1.83 (0.85–3.98)	1.96 (0.99–3.88)
	Predominantly pipe	1.17 (0.15–8.76)	1.16 (0.31–4.30)	1.16 (0.39–3.51)
	Exclusive pipe	1.34 (0.31–5.79)	1.37 (0.24–7.68)	1.35 (0.44–4.14)
Pancreas	Predominantly cigar	1.98 (0.60–6.46)	0.50 (0.06–4.12)	1.64 (0.53–5.09)
	Exclusive cigar	1.71 (0.23–12.59)	1.60 (0.40–6.30)	1.42 (0.51–4.01)
	Predominantly pipe	0.58 (0.08–4.22)	3.70 (0.92–14.83)	2.01 (0.64–6.27)
	Exclusive pipe	1.02 (0.31–3.33)	[a]	[b]
Kidney	Predominantly cigar	1.46 (0.20–10.59)	0.95 (0.26–3.43)	1.08 (0.37–3.18)
	Exclusive cigar	1.56 (0.48–5.02)	1.88 (0.73–4.81)	1.75 (0.84–3.64)
	Predominantly pipe	1.97 (0.71–5.50)	2.41 (0.73–7.99)	2.15 (0.99–4.67)
	Exclusive pipe	1.31 (0.52–3.29)	[a]	[b]
Bladder	Predominantly cigar	[a]	1.91 (0.82–4.46)	[b]
	Exclusive cigar	[a]	1.89 (0.19–3.60)	[b]
	Predominantly pipe	0.62 (0.08–4.59)	4.38 (1.77–10.84)	3.16 (1.38–7.23)
	Exclusive pipe	0.75 (0.18–3.14)	3.60 (0.88–14.65)	1.67 (0.61–4.54)
Colorectal	Predominantly cigar	1.81 (0.57–5.74)	1.12 (0.63–1.99)	1.23 (0.74–2.06)
	Exclusive cigar	1.64 (0.76–3.55)	0.97 (0.55–1.69)	1.16 (0.74–1.83)
	Predominantly pipe	0.64 (0.20–2.02)	1.36 (0.64–2.87)	1.09 (0.58–2.04)
	Exclusive pipe	0.96 (0.47–1.99)	1.76 (0.57–5.44)	1.15 (0.62–2.10)
All cancers[c]	Predominantly cigar	0.97 (0.40–2.35)	1.34 (0.85–2.11)	1.25 (0.84–1.88)
	Exclusive cigar	1.7 (1.14–2.68)	1.12 (0.72–1.72)	1.41 (1.04–1.91)
	Predominantly pipe	0.95 (0.56–1.62)	1.87 (1.03–3.40)	1.28 (0.86–1.91)
	Exclusive pipe	1.19 (0.82–1.73)	1.69 (0.64–4.45	1.25 (0.88–1.76)

NOTE: All analyses adjusted for age at enrollment, gender, body mass index at enrollment, race/ethnicity, socioeconomic status, average alcohol intake, and family history of specific cancer (and history of chronic lung disease for lung cancer analysis, history for chronic liver disease for liver cancer analysis). Never smokers—referent category.

[a]No cancer cases reported in this category.

[b]Combined HR not calculated as only one study with HR calculated.

[c]All cancer incidence calculated for all cancers including prostate cancer.

number of cases in exclusive cigar and pipe smokers, but we note that this analysis had the largest sample size to date. Moreover, the studies included in this analysis are cohort studies and therefore are less susceptible to selection and reporting bias compared with case–control studies. Another asset of our study was detailed information on important covariates. Limitations of our study include that none of the cohorts included had detailed data on other tobacco products such as cigarillos, hookahs, or smokeless tobacco. Cohort members also tended to be more educated and had healthier lifestyles than the source populations. Also, there was some degree of heterogeneity in the data collected by each study on smoking and potential confounders. Because information on grams of tobacco smoked was not available, we had to use conversions based on estimates of the average weight of tobacco in each smoking product for lifetime consumption analyses. This may not reflect fluctuations in the duration and frequency of smoking across the life span. Also we had detailed data about smoking variables such as age of initiation and cessation of each product only for the VITAL and NLCS studies as other studies have not collected this information. Finally, we had too few women users of these products to study the effects in women. Another limitation could be the variation in the size and chemical characteristics of cigars and pipes between the countries where the studies included in the pooled analyses were conducted. However, these tobacco products are relatively homogeneous within each country (9). Therefore, adjustment by study/country, which was performed in all analyses reported in the article, reduces the opportunity for bias.

The pooled analysis of data from five prospective cohorts in this analysis highlights the increased risk for smoking-related cancers, particularly for lung and head and neck cancers in exclusive smokers (former and current) of cigars and pipe. Based on these significant findings, there is an urgent need to focus on efforts to increase awareness about health hazards from these products and to modify present prevention efforts to reduce exposure to all tobacco products.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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Conception and design: J. Malhotra, C.C. Abnet, G.G. Giles, P. Boffetta
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