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ARTICLE

Contemporary Associations of Exclusive Cigarette, Cigar, Pipe, and Smokeless Tobacco Use With Overall and Cause-Specific Mortality in the United States

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Abstract

Background: A growing proportion of tobacco users in the United States use non-cigarette products including cigars, pipes, and smokeless tobacco. Studies examining the disease and mortality risks of these products are urgently needed.
Methods: We harmonized tobacco use data from 165 335 adults in the 1991, 1992, 1998, 2000, 2005, and 2010 National Health Interview Surveys. Hazard ratios (HRs) and 95% confidence intervals (CIs) for overall and cause-specific mortality occurring through December 31, 2015, were estimated by exclusive use of cigarettes, cigars, pipes, or smokeless tobacco using Cox proportional hazards regression with age as the underlying time metric and never tobacco users as the referent group.
Results: Current use of cigarettes (HR = 2.23, 95% CI = 2.13 to 2.33) and smokeless tobacco (HR = 1.36, 95% CI = 1.17 to 1.59) were each associated with overall mortality. Relative to never tobacco users, higher risks were observed both in daily (HR = 2.34, 95% CI = 2.24 to 2.44) and nondaily (HR = 1.69, 95% CI = 1.54 to 1.86) cigarette smokers, with associations also observed across major smoking-related causes of death. Daily use of smokeless tobacco was also associated with overall mortality (HR = 1.41, 95% CI = 1.20 to 1.66) as was daily use of cigars (HR = 1.52, 95% CI = 1.12 to 2.08). Current smokeless tobacco use was associated with a higher risk of mortality from heart disease and smoking-related cancer, with strong associations observed for cancers of the oral cavity and bladder.
Conclusions: Exclusive daily use of cigarettes, cigars, and smokeless tobacco was associated with higher mortality risk. Tobacco control efforts should include cigars and smokeless tobacco.

Tobacco remains the leading cause of chronic disease and death in the United States and worldwide (1). Cigarettes are the most commonly used tobacco product and are estimated to cause nearly 500 000 deaths per year in the United States alone (1). Nevertheless, a growing proportion of US tobacco users use non-cigarette tobacco products including cigars, pipes, and smokeless tobacco (2,3). Nationally representative data from the 2017 US National Health Interview Survey (NHIS) indicate that 34.3 million (14.0%) US adults currently use cigarettes; 9.3 million (3.8%) use cigars, cigarillos, or filtered little cigars; 5.1 million (2.1%) use smokeless tobacco; and 2.6 million (1.0%) use pipes or water pipes (2).

Cigarettes are known to cause many types of cancer, cardiovascular disease, and other diseases. Less is known, however, about the risks of non-cigarette tobacco products. Cigars and pipes have been determined to cause many of the same diseases as cigarettes, including cancers of the oral cavity, esophagus, pancreas, larynx, and lung, and coronary heart disease (CHD) (4). Smokeless tobacco has been determined to cause cancers of the oral cavity, esophagus, and pancreas, although

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associations with other endpoints including cardiovascular disease and cancers such as lung cancer are less clear. Prior studies of non-cigarette tobacco products are limited by a lack of information on usage patterns (eg, current vs former, daily vs nondaily). Existing cohort studies also tend to be decades old and may not reflect the disease risks of current products or usage patterns. In the United States, only a few prospective studies have examined disease risks (5–8), and even data from case-control studies are sparse (9–11).

The prevalence of smokeless tobacco use may increase in the future. Several tobacco manufacturers are applying to the US Food and Drug Administration to classify and market particular smokeless tobacco products as Modified Risk Tobacco Products, arguing that they have lower toxicity than cigarettes. Concurrently, the Food and Drug Administration has recently proposed to reduce the nicotine content of cigarettes in the US market. Such efforts may increase cessation rates among cigarette smokers but may also encourage cigarette smokers to switch to forms of tobacco with higher nicotine content.

To inform tobacco regulation, it is essential to have robust estimates as to the disease and mortality risks of cigars, pipes, and smokeless tobacco products in the United States. Therefore, we examined associations of daily and nondaily use of cigarettes and non-cigarette tobacco products with mortality by pooling data from the 1991, 1992, 1998, 2000, 2005, and 2010 NHIS surveys with available follow-up through December 31, 2015.

Methods

National Health Interview Survey

The NHIS is an annual national household survey that collects comprehensive information on demographics, behaviors, socioeconomic status, and health status among the civilian noninstitutionalized population in the United States. Each year, households across the United States are randomly selected using a complex stratified multistage cluster sample design, with sample weights to account for differential sampling and nonresponse rates of sampled persons and poststratification adjustments to US population totals. Detailed information on the NHIS, including informed consent procedures, and its publicly available data can be found at the NHIS website (http://www.cdc.gov/nchs/nhis.htm).

Tobacco Use Assessment

Each NHIS survey includes supplements that address current public health concerns. Tobacco use questionnaires for adults aged 18 years and older have been included in the supplements since 1965.

Tobacco use was assessed using publicly available data from the 1991 Health Promotion and Disease Prevention Supplement, the 1992 Cancer Epidemiology Supplement, and the core NHIS survey in 1998, 2000, 2005, and 2010, which assessed daily and nondaily use of cigarettes and non-cigarette tobacco products. Response rates to the tobacco questionnaires ranged from 61% in 2010 to 88% in 1991. Tobacco use questions were mostly consistent across each included survey. We combined them into a single dataset for analyses. A list of tobacco use topics by year is available on the NHIS website.

Participants who reported ever using at least 100 cigarettes, cigars 50 times, pipes 50 times, chewing tobacco 20 times, or snuff 20 times in their lifetime were identified as ever-users. Chewing tobacco and snuff were combined as smokeless tobacco, because previous data indicate that respondents have difficulty accurately recalling the forms of smokeless tobacco that they use (12). Ever-users who reported currently using a tobacco product were identified as current users and categorized into those who used every day (daily users) or on some days (nondaily users). We identified participants who reported using a single form of tobacco in their life (exclusive users). Participants who reported ever using two or more tobacco products (9.4%) were not analyzed further. We defined former users as participants who had ever used but did not currently use a product. Participants who reported never using cigarettes, cigars, pipes, and smokeless tobacco served as the referent group (never tobacco users).

Mortality Ascertainment

The NHIS has been linked to the National Death Index that provides date and cause of death ascertained from death certificates. On average, 95% of the NHIS participants were eligible for the mortality follow-up (13). We identified deaths through December 31, 2015, using the recently expanded restricted-use NHIS-Linked Mortality Files. We examined overall and cause-specific mortality from smoking-related causes of death identified by International Classification of Diseases version 10 codes, including cancer (C00-C97), heart disease (I00-I09, I11, I13, I20-I51), chronic lower respiratory disease (J40-J47), and cerebrovascular disease (I60-I69). We also examined mortality from smoking-related cancers combined and individually, including cancers of the lip, oral cavity and pharynx (C00-C14), esophagus (C15), stomach (C16), colon, rectum, and anus (C18-C21), liver and intrahepatic bile duct (C22), pancreas (C25), larynx (C32), trachea, bronchus, and lung (C33-C34), cervix uteri (C53), kidney and renal pelvis (C64-C65), and bladder (C67).

Statistical Analysis

Among 179 166 adults (≥18 years) who completed the surveys, we excluded 6915 who were not eligible for mortality data linkage, 48 with missing or incomplete birth date, 5 with missing or incomplete interview date, 22 who were younger than 18 years, and 193 who were older than 95 years at the time of the survey. We also excluded 6648 individuals with missing tobacco data, resulting in a total of 165 335 individuals (1991, 41 378; 1992, 11 606; 1998, 30 109; 2000, 29 619; 2005, 27 668; and 2010, 24 955) in our analytic cohort.

Participants were followed up from the date of the survey through the date of death, the date before they turned 96 years old, or December 31, 2015, whichever occurred first. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using multivariable-adjusted Cox proportional hazards regression, with age as the underlying time metric and adjusted for sex, race or ethnicity, education, and survey year. Baseline hazards in the Cox models were stratified by 5-year birth cohort. Additional adjustments for family income and alcohol intake did not change the results for all-cause mortality considerably; thus, these factors were not included in further analyses. An indicator was assigned for missing values. Because pipe use was not assessed in the 2010 survey, we did not include the 2010 data in analyses of pipe use. Analyses of cigarettes, smokeless tobacco, and cigars included a sensitivity analysis excluding the 2010 data. Analyses were conducted using SAS-callable SUDAAN

release 11.0.1. Hazard ratios were determined to be statistically different than 1 when the 95% confidence intervals excluded 1; no adjustment was made for multiple comparisons. All analyses accounted for the complex sample design and sample weights of the NHIS.

Results

Our participants consisted of 71 314 men (weighted percentage, 47.9%) and 94 021 women (52.1%) who were predominantly non-Hispanic white (73.9%), followed by non-Hispanic black (11.2%), Hispanic (10.7%), and other (4.1%). About 51.1% of study participants reported never using tobacco products. The prevalence of exclusive use of each tobacco product was 19.9% (cigarettes), 0.9% (smokeless tobacco), 0.4% (cigars), and 0.1% (pipes). About 55% of current and former exclusive cigarette smokers were women, whereas a majority of current and former exclusive users of other tobacco products (89–99%) were men (Table 1). Compared with current users of cigarettes and cigars, current users of pipes and smokeless tobacco were more likely to be non-Hispanic white. Higher proportions of current cigar and pipe users had a college or graduate school education than current users of cigarettes and smokeless tobacco.

In our analysis, 62 706 participants were exclusive ever-cigarette smokers. The proportion of daily users among current users of each tobacco product was 82.0% (cigarettes), 22.8% (cigars), 67.2% (pipes), and 66.0% (smokeless tobacco). Current (HR = 2.23, 95% CI = 2.13 to 2.33) and former cigarette smokers (HR = 1.33, 95% CI = 1.28 to 1.37) had higher mortality risk than never tobacco users (Table 2). Among current cigarette smokers, higher risk was observed among daily smokers (HR = 2.34, 95% CI = 2.24 to 2.44) than nondaily smokers (HR = 1.69, 95% CI = 1.54 to 1.86). A weaker but still elevated mortality risk was observed among former cigarette smokers (HR = 1.33, 95% CI = 1.28 to 1.37). Similar associations were observed in men and women.

There were 2547 exclusive ever-users of smokeless tobacco. Current smokeless tobacco use was associated with a higher mortality risk (HR = 1.36, 95% CI = 1.17 to 1.59) than never use of tobacco, with higher risks observed among daily (HR = 1.41, 95% CI = 1.20 to 1.66) but not nondaily users. Former use of smokeless tobacco was not statistically significantly associated with mortality.

Fewer exclusive cigar smokers were available for analysis (n = 1595). Overall, current use was not associated with mortality. An increased risk was observed with current daily (HR = 1.52, 95% CI = 1.12 to 2.08) but not current nondaily use. No association was observed for former cigar use. We observed no association with pipe smoking, although just 102 participants (27 deaths) were exclusive current pipe smokers.

Current cigarette use was associated with all causes of death examined, with especially strong associations observed for chronic lower respiratory disease (HR = 12.24, 95% CI = 10.1 to 14.96) and smoking-related cancers combined (HR = 4.94, 95% CI = 4.41 to 5.53) relative to never tobacco use (Tables 3). Among cancers, the strongest associations were observed for lung cancer (daily: HR = 16.77, 95% CI = 13.65 to 20.59; nondaily: HR = 8.73, 95% CI = 6.25 to 12.19) (Table 4).

Current smokeless tobacco use was associated with an increased risk of mortality from heart disease (HR = 1.63, 95% CI = 1.27 to 2.09), especially among daily users (HR = 1.76, 95% CI = 1.34 to 2.30), all cancer (HR = 1.48, 95% CI = 1.04 to 2.12), and smoking-related cancer (HR = 1.76, 95% CI = 1.07 to 2.90). Associations with current use were particularly striking for cancers of the oral cavity (HR = 8.81, 95% CI = 1.45 to 53.66) and bladder (HR = 6.56, 95% CI = 1.00 to 42.95), especially among daily users (HR = 9.89 for oral cavity and 8.44 for bladder). Hazard ratios were also elevated, but not statistically significant for cancers of the lung (HR = 2.68, 95% CI = 0.95 to 7.51), pancreas (HR = 1.55, 95% CI = 0.48 to 4.97), esophagus (HR = 1.29, 95% CI = 0.16 to 10.52), and colon and rectum (HR = 1.27, 95% CI = 0.50 to 3.24), although the number of deaths was small for these endpoints.

Current cigar users generally had increased mortality risks, although most risk estimates were not statistically significant with sparse numbers of deaths. Associations tended to be stronger for daily cigar use than for nondaily use. Hazard ratios were elevated, but not statistically significant, for cancers of the oral cavity (HR = 1.77, 95% CI = 0.24 to 12.87), lung (HR = 2.68, 95% CI = 0.95 to 7.51), and bladder (HR = 3.87, 95% CI = 0.50 to 29.74).

The observed all-cause mortality associations did not change after additional adjustment for alcohol intake and household income. In a sensitivity analysis, similar associations were observed for cigarettes, cigars, and smokeless tobacco after excluding the 2010 data (data not shown).

Discussion

In this large nationally representative study of US adults, current exclusive users of cigarettes and smokeless tobacco had a higher mortality risk than never tobacco users, with stronger associations observed for daily use than nondaily use. Daily users of cigars also had a higher risk of mortality. Our findings confirm previously reported substantial disease risks for both daily and nondaily cigarette smoking (14–17) and provide much needed information on mortality risks among users of contemporary cigar and smokeless tobacco products.

One key finding of the current study is an increased mortality risk among users of US smokeless tobacco products. A comprehensive review conducted by the International Agency for Research on Cancer (IARC) concluded that smokeless tobacco causes cancers of the oral cavity, esophagus, and pancreas in humans (17,18). Supporting IARC's findings, exclusive use of smokeless tobacco was strongly associated with mortality from oral cavity cancer in the current study. For esophageal and pancreatic cancer, the hazard ratios were above 1, although not statistically significant with few deaths. Stronger associations were observed among daily than nondaily users, and no associations were observed for former users. However, few US prospective studies have been conducted; these studies were limited by a low prevalence of smokeless tobacco use, few numbers of exclusive users of smokeless tobacco, and limited characterization of usage patterns (5,9–11). In addition, most of these studies were conducted decades ago and may not reflect contemporary products.

Previous studies generally observed an increased mortality risk for smokeless tobacco use, although most of the studies were conducted in southeast Asia or Sweden. A recent meta-analysis identified 16 cohorts and observed a summary mortality risk estimate of 1.22 (95% CI = 1.11 to 1.34) (19). However, harmful constituents of smokeless tobacco products differ substantially by regions (20), and fewer studies have been conducted in the United States. In the Cancer Prevention Study II (CPS-II), current exclusive users of smokeless tobacco had higher mortality risks from all causes (HR = 1.18, 95% CI = 1.08 to 1.29), as did participants in the Cancer Prevention Study I

Table 1. Sample sizes and weighted proportions (standard errors) of demographic characteristics among 165 335 participants of the National Health Interview Surveys and by exclusive use of tobacco products

			Type of tobacco use							
			Exclusive use							
			Cigarettes		Cigars		Pipes†		Smokeless tobacco	
Characteristic	All*	Never use of any tobacco product	Current	Former	Current	Former	Current	Former	Current	Former
Total	165 335	84 419	32 865	29 841	728	867	102	345	1465	1082
Age, y										
18–24	17 559	11 298	3593	1061	70	40	7	5	269	158
%	13.1 (0.2)	16.7 (0.2)	13.6 (0.3)	4.3 (0.2)	10.2 (1.5)	6.0 (1.1)	6.2 (3.1)	2.6 (1.6)	21.3 (1.5)	16.3 (1.6)
25–34	33 640	19 085	7836	3524	126	89	10	21	433	336
%	19.9 (0.1)	21.8 (0.2)	23.4 (0.3)	12.0 (0.2)	15.4 (1.5)	9.9 (1.2)	9.3 (3.3)	5.3 (1.3)	30.6 (1.5)	31.7 (1.8)
35–44	33 604	17 033	8030	5069	174	138	11	61	298	267
%	20.6 (0.1)	20.4 (0.2)	24.4 (0.3)	17.6 (0.3)	25.2 (1.9)	16.2 (1.6)	11.7 (4.3)	17.3 (2.4)	21.6 (1.3)	24.9 (1.5)
45–64	48 299	21 188	10 232	10 935	260	276	39	147	226	193
%	30.0 (0.2)	26.0 (0.2)	30.9 (0.4)	38.7 (0.4)	37.5 (2.1)	33.3 (2.0)	40.4 (5.8)	45.0 (3.2)	16.0 (1.4)	20.1 (1.5)
65–95	32 233	15 815	3174	9252	98	324	35	111	239	128
%	16.4 (0.2)	15.2 (0.2)	7.8 (0.2)	27.5 (0.3)	11.7 (1.3)	34.7 (2.0)	32.6 (4.8)	29.8 (2.8)	10.6 (0.9)	7.1 (0.8)
Sex										
Male	71 314	28 619	13 200	12 654	695	817	97	341	1198	928
%	47.9 (0.2)	38.7 (0.2)	44.3 (0.4)	46.0 (0.4)	97.1 (0.6)	95.5 (0.8)	96.0 (2.0)	98.6 (0.8)	88.7 (1.1)	90.4 (1.0)
Female	94 021	55 800	19 665	17 187	33	50	5	4	267	154
%	52.1 (0.2)	61.3 (0.2)	55.7 (0.4)	54.0 (0.4)	2.9 (0.6)	4.5 (0.8)	4.0 (2.0)	1.5 (0.8)	11.3 (1.1)	9.6 (1.0)
Race or ethnicity										
Non-Hispanic white	112 881	52 153	22 828	22 805	511	679	87	291	1167	872
%	73.9 (0.3)	67.7 (0.3)	75.2 (0.4)	81.2 (0.3)	77.3 (1.8)	82.5 (1.6)	88.5 (3.4)	85.9 (2.3)	85.8 (1.3)	86.9 (1.2)
Non-Hispanic black	22 862	12 861	5271	3027	137	77	7	25	218	116
%	11.2 (0.2)	12.9 (0.2)	12.7 (0.3)	7.8 (0.2)	14.5 (1.5)	7.4 (1.0)	4.6 (2.1)	5.8 (1.6)	9.3 (1.1)	6.5 (0.9)
Hispanic	23 226	15 206	3785	3189	68	99	4	21	42	72
%	10.7 (0.2)	13.9 (0.3)	8.7 (0.3)	8.1 (0.2)	6.7 (1.0)	9.2 (1.1)	2.2 (1.2)	4.7 (1.2)	2.2 (0.4)	4.9 (0.7)
Non-Hispanic other	6188	4097	939	801	12	12	4	7	36	21
%	4.1 (0.1)	5.4 (0.2)	3.3 (0.2)	2.8 (0.2)	1.5 (0.6)	0.9 (0.3)	4.7 (2.4)	3.0 (1.2)	2.5 (0.5)	1.7 (0.5)
Education										
<High school	33 427	15 751	7912	5630	90	143	10	31	408	164
%	17.9 (0.2)	15.8 (0.2)	22.8 (0.3)	16.4 (0.3)	9.9 (1.2)	14.7 (1.6)	7.8 (2.8)	8.2 (1.6)	23.7 (1.4)	12.1 (1.4)
High school	51 429	23 747	12 463	9358	194	202	32	61	442	259
%	31.7 (0.2)	28.3 (0.2)	39.3 (0.4)	32.2 (0.3)	24.2 (1.9)	23.1 (1.8)	39.3 (8.3)	18.6 (2.5)	32.7 (1.6)	24.9 (1.8)
Some college	42 879	21 906	8559	7895	178	197	25	83	372	316
%	26.5 (0.2)	26.8 (0.2)	26.1 (0.3)	27.0 (0.3)	24.7 (2.0)	24.9 (1.8)	17.9 (3.8)	23.8 (2.8)	26.1 (1.5)	29.7 (1.7)
College	23 223	14 130	2641	4140	152	151	19	82	176	235
%	14.9 (0.1)	18.1 (0.2)	8.1 (0.2)	14.7 (0.3)	22.1 (1.9)	17.7 (1.5)	22.9 (5.8)	24.8 (2.8)	12.5 (1.1)	22.8 (1.6)
Graduate school	13 734	8528	1169	2706	111	174	16	87	63	108
%	8.6 (0.1)	10.7 (0.2)	3.3 (0.1)	9.3 (0.2)	18.9 (1.9)	19.5 (1.6)	12.1 (3.5)	24.2 (2.7)	4.6 (0.6)	10.5 (1.2)
Survey										
1991	41 378	19 382	9082	7043	81	111	45	107	474	222
Row %	100.0	46.6 (0.4)	21.1 (0.3)	16.7 (0.2)	0.2 (0.0)	0.3 (0.0)	0.1 (0.0)	0.3 (0.0)	1.3 (0.1)	0.6 (0.1)
1992	11 606	5455	2529	1931	26	28	6	27	119	83
Row %	100.0	46.4 (0.6)	21.0 (0.4)	16.4 (0.4)	0.2 (0.1)	0.3 (0.1)	0.1 (0.0)	0.3 (0.1)	1.1 (0.1)	0.9 (0.1)
1998	30 109	14 867	5964	5282	105	74	12	78	233	264
Row %	100.0	49.1 (0.4)	19.4 (0.3)	17.1 (0.3)	0.4 (0.0)	0.3 (0.0)	0.0 (0.0)	0.3 (0.0)	0.9 (0.1)	1.0 (0.1)
2000	29 619	15 324	5824	5174	110	100	19	70	236	133
Row %	100.0	50.9 (0.4)	19.3 (0.3)	17.3 (0.3)	0.4 (0.0)	0.4 (0.0)	0.1 (0.0)	0.3 (0.0)	1.0 (0.1)	0.6 (0.1)
2005	27 668	14 846	4746	4714	120	107	20	63	183	159
Row %	100.0	53.7 (0.4)	16.8 (0.3)	16.3 (0.3)	0.5 (0.1)	0.4 (0.1)	0.1 (0.0)	0.2 (0.0)	0.8 (0.1)	0.7 (0.1)
2010	24 955	14 098	3893	4240	136	154	NA†	NA	199	187
Row %	100.0	55.4 (0.4)	15.4 (0.3)	16.8 (0.3)	0.6 (0.1)	0.6 (0.1)	NA	NA	1.1 (0.1)	0.9 (0.1)

*A total number includes participants who reported ever-using two or more tobacco products (9.4% of a study population).
†Pipe use data were not collected in the 2010 survey.

Table 2. All-cause mortality by exclusive use status of cigarettes, cigars, pipes, and smokeless tobacco

	Cigarettes		Cigars		Pipes*		Smokeless tobacco†	
	Death	HR (95% CI)‡	Death	HR (95% CI)‡	Death	HR (95% CI)‡	Death	HR (95% CI)‡
All								
Never tobacco user§	12 830	1.00	12 830	1.00	12 084	1.00	12 830	1.00
Former	8208	1.33 (1.28 to 1.37)	249	1.00 (0.83 to 1.20)	90	0.86 (0.67 to 1.10)	134	1.17 (0.92 to 1.49)
Current	7123	2.23 (2.13 to 2.33)	121	1.16 (0.94 to 1.43)	27	0.91 (0.60 to 1.40)	275	1.36 (1.17 to 1.59)
Daily	6197	2.34 (2.24 to 2.44)	54	1.52 (1.12 to 2.08)	19	0.92 (0.57 to 1.47)	214	1.41 (1.20 to 1.66)
Nondaily	926	1.69 (1.54 to 1.86)	67	0.96 (0.72 to 1.28)	8	0.91 (0.37 to 2.26)	61	1.20 (0.84 to 1.71)
Additional adjustment for alcohol and household income‖								
Never tobacco user§	12 830	1.00	12 830	1.00	12 084	1.00	12 830	1.00
Former	8208	1.37 (1.33 to 1.42)	249	1.05 (0.88 to 1.26)	90	0.85 (0.65 to 1.10)	134	1.16 (0.91 to 1.48)
Current	7123	2.25 (2.16 to 2.35)	121	1.21 (0.97 to 1.49)	27	0.95 (0.62 to 1.45)	275	1.33 (1.14 to 1.54)
Daily	6197	2.35 (2.25 to 2.46)	54	1.53 (1.10 to 2.13)	19	0.95 (0.59 to 1.51)	214	1.37 (1.16 to 1.61)
Nondaily	926	1.74 (1.58 to 1.92)	67	1.02 (0.76 to 1.36)	8	0.95 (0.38 to 2.33)	61	1.19 (0.83 to 1.70)
Men								
Never tobacco user§	3460	1.00	3460	1.00	3127	1.00	3460	1.00
Former	3953	1.31 (1.24 to 1.39)	243	1.00 (0.83 to 1.20)	90	0.88 (0.69 to 1.12)	88	1.20 (0.89 to 1.63)
Current	3042	2.20 (2.06 to 2.36)	¶	1.13 (0.91 to 1.39)	¶	0.91 (0.59 to 1.39)	132	1.33 (1.08 to 1.65)
Daily	2659	2.30 (2.14 to 2.46)	¶	1.46 (1.07 to 1.99)	¶	0.89 (0.55 to 1.43)	100	1.41 (1.12 to 1.78)
Nondaily	383	1.71 (1.47 to 1.99)	67	0.95 (0.71 to 1.27)	8	1.02 (0.41 to 2.53)	32	1.10 (0.69 to 1.74)
Women								
Never tobacco user§	9370	1.00	9370	1.00	8957	1.00	9370	1.00
Former	4255	1.35 (1.29 to 1.41)	6	3.96 (1.44 to 10.84)	0	NA	46	1.03 (0.71 to 1.49)
Current	4081	2.27 (2.15 to 2.39)	¶	3.71 (1.32 to 10.41)	¶	1.64 (0.13 to 21.34)	143	1.37 (1.11 to 1.69)
Daily	3538	2.40 (2.27 to 2.53)	¶	7.48 (3.30 to 16.98)	¶	12.06 (1.16 to 125.77)	114	1.37 (1.08 to 1.72)
Nondaily	543	1.69 (1.49 to 1.91)	0	NA	0	NA	29	1.35 (0.83 to 2.18)

*Pipe use data were not collected in the 2010 survey and thus the analysis excluded data from the 2010 survey. CI = confidence interval; HR = hazard ratio; NA, not applicable.

†Chewing tobacco and snuff.

‡Adjusted for sex, education level (<high school, high school, some college or associate degree, college, graduate or professional school, and missing), race or ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, non-Hispanic other, and missing), and survey year (1991, 1992, 1998, 2000, 2005, and 2010) using age at survey as the underlying time metric. Baseline hazards in the Cox models were stratified by 5-year birth cohort.

§For cigarettes, cigars, and smokeless tobacco columns, "Never tobacco user" means never used cigarettes, cigars, or smokeless tobacco. For the pipe column, "Never tobacco user" means never used cigarettes, cigars, smokeless tobacco, or pipes.

‖Additionally adjusted for alcohol intake (none, >0–0.5, >0.5–1, >1–3, >3–5, and >5 drinks per day, and missing) and ratio of family income to poverty level (<1.00, 1.00–1.99, 2.00–3.99, ≥4.00, and missing).

¶Values are suppressed for confidentiality of fewer than five individuals.

(CPS-I) (HR = 1.18, 95% CI = 1.11 to 23) (5). However, no association was observed between smokeless tobacco use and mortality in a recent analysis using the Tobacco Use Supplement to the Current Population Survey (TUS-CPS) between 1985 and 2011 (14).

A number of previous studies have observed associations between smokeless tobacco and CHD, but their findings are considered inconclusive (5,6,8,14). Many previous studies were unable to examine the association among exclusive smokeless tobacco users or current vs former use. In published cohort studies, the hazard ratios were 1.18 (95% CI = 1.11 to 1.21) in CPS-I (5), 1.26 (95% CI = 1.08 to 1.47) in CPS-II (5), and 1.24 (95% CI = 1.05 to 1.46) in the TUS-CPS analysis (14). Several potential mechanisms lend plausibility to an association between smokeless tobacco use and CHD; for example, smokeless tobacco in the United States contains as much nicotine as cigarettes (15). Nicotine and other constituents from smokeless tobacco have been associated with increased blood pressure, hypercholesterolemia, a reduction in high-density lipoprotein, and inflammation (15). Observations of a stronger association among daily than nondaily current users in our study provide further evidence for an association.

We also observed higher mortality risks for bladder cancer among current smokeless tobacco users, especially daily users. Tobacco smoking, including cigarettes, cigars, and pipes, has been shown to cause bladder cancer (1,4,16). To date, however, few studies have examined the association of smokeless tobacco with bladder cancer (20). Previous studies have generally been unable to restrict their analysis to exclusive smokeless tobacco users and have had small numbers of cases (11).

We observed some evidence for an association between smokeless tobacco and lung cancer. In CPS-II, the hazard ratio for current exclusive use of smokeless tobacco relative to never tobacco use was 2.00 (95% CI = 1.23 to 3.24) (5). A similar association was observed for exclusive ever-use in the Agricultural Health Study (HR = 2.21, 95% CI = 1.11 to 4.42) (21). However, no association was observed in CPS-I (5). An association between smokeless tobacco and lung cancer is plausible because smokeless tobacco products have high levels of tobacco-specific nitrosamines, such as 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, a strong lung carcinogen (18).

Cigar and pipe smoking were previously associated with an increased mortality risk, although previous studies have limitations including a low prevalence of exclusive use and small numbers of deaths. In a recent analysis of the TUS-CPS, the hazard ratios for current exclusive cigar use vs never tobacco use were 1.20 (95% CI = 1.03 to 1.38) for all-cause, 1.61 (95% CI = 1.11 to 2.32) for all smoking-related cancer, and 3.26 (95% CI =

Table 3. Cause-specific mortality by exclusive daily or nondaily use of cigarettes, cigars, or smokeless tobacco among current tobacco users with never tobacco users as a referent group

Characteristic	Coronary heart disease	Chronic lower respiratory disease	Cerebrovascular disease	Cancer	Smoking-related cancer*
No. of deaths	8950	1889	2046	7921	4575
Never tobacco use, No. of deaths	3626	264	995	2552	1058
HR	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Cigarettes					
Former, No. of deaths	2250	616	466	1969	1136
HR (95% CI)†	1.22 (1.14 to 1.31)	4.41 (3.62 to 5.37)	0.96 (0.83 to 1.11)	1.54 (1.42 to 1.66)	2.10 (1.88 to 2.35)
Current, all, No. of deaths	1597	698	327	2110	1532
HR (95% CI)	1.94 (1.78 to 2.11)	12.24 (10.1 to 14.96)	1.57 (1.32 to 1.86)	2.79 (2.57 to 3.04)	4.94 (4.41 to 5.53)
Current, daily, No. of deaths	1370	627	274	1880	1374
HR (95% CI)	2.01 (1.83 to 2.20)	13.04 (10.64 to 15.99)	1.58 (1.32 to 1.90)	2.96 (2.71 to 3.23)	5.27 (4.69 to 5.92)
Current, nondaily, No. of deaths	227	71	53	230	158
HR (95% CI)	1.58 (1.33 to 1.88)	8.06 (5.53 to 11.76)	1.49 (1.06 to 2.08)	1.98 (1.65 to 2.37)	3.25 (2.60 to 4.05)
Cigars					
Former, No. of deaths	82	‡	13	43	21
HR (95% CI)	1.12 (0.81 to 1.54)	0.91 (0.27 to 3.08)	0.58 (0.30 to 1.12)	0.88 (0.61 to 1.27)	0.91 (0.54 to 1.52)
Current, all, No. of deaths	35	‡	7	33	13
HR (95% CI)	1.24 (0.83 to 1.85)	1.05 (0.30 to 3.69)	1.12 (0.51 to 2.49)	1.50 (0.98 to 2.31)	1.12 (0.61 to 2.07)
Current, daily, No. of deaths	17	‡	‡	16	6
HR (95% CI)	1.32 (0.76 to 2.30)	2.14 (0.48 to 9.53)	1.71 (0.59 to 4.94)	2.27 (1.23 to 4.19)	1.98 (0.84 to 4.67)
Current, nondaily, No. of deaths	18	‡	‡	17	7
HR (95% CI)	1.20 (0.69 to 2.07)	0.38 (0.05 to 2.80)	0.74 (0.23 to 2.42)	1.14 (0.63 to 2.08)	0.71 (0.31 to 1.59)
Smokeless tobacco§					
Former, No. of deaths	52	‡	10	19	10
HR (95% CI)	1.50 (1.04 to 2.17)	0.11 (0.02 to 0.82)	0.72 (0.33 to 1.54)	0.93 (0.52 to 1.67)	1.30 (0.57 to 2.98)
Current, all, No. of deaths	91	5	20	51	26
HR (95% CI)	1.63 (1.27 to 2.09)	1.57 (0.53 to 4.69)	1.16 (0.62 to 2.18)	1.48 (1.04 to 2.12)	1.76 (1.07 to 2.90)
Current, daily, No. of deaths	71	5	‡	40	20
HR (95% CI)	1.76 (1.34 to 2.30)	1.87 (0.63 to 5.57)	1.24 (0.62 to 2.49)	1.37 (0.92 to 2.04)	1.61 (0.85 to 3.04)
Current, nondaily, No. of deaths	20	0	‡	11	6
HR (95% CI)	1.10 (0.61 to 1.96)	NA	0.79 (0.26 to 2.40)	1.91 (0.98 to 3.75)	2.40 (0.96 to 6.04)

*Smoking-related cancers include cancers of the lip, oral cavity, pharynx, esophagus, stomach, colon, rectum, anus, liver and intrahepatic bile duct, pancreas, larynx, trachea, bronchus, lung, cervix uteri, kidney, rectal pelvis, and bladder. CI = confidence interval; HR = hazard ratio; NA, not applicable.

†Adjusted for sex, education level (<high school, high school, some college or associated degree, college, graduate or professional school, and missing), race or ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, non-Hispanic other, and missing), and survey year (1991, 1992, 1998, 2000, 2005, and 2010) using age at survey as the underlying time metric. Baseline hazards in the Cox models were stratified by 5-year birth cohort.

‡Values are suppressed for confidentiality of fewer than five individuals.

§Chewing tobacco and snuff.

1.86 to 5.71) for lung cancer mortality (22). Results for cigar smoking in the current analysis support these prior results.

This study has several strengths. By applying survey weights in the analysis of a nationally representative sample of US adults with a nearly complete follow-up, our findings are representative of the US civilian adult population. Using detailed tobacco use information, we were able to identify exclusive users of each tobacco product and examine risks by daily and nondaily use. By harmonizing multiple surveys, the large sample size enabled examination of a broad range of smoking-related mortality outcomes. Finally, our study used tobacco use data collected in 1991–2010 with follow-up through 2015, providing contemporary mortality risk estimates of tobacco products.

There are also limitations. Although we harmonized multiple surveys, we had limited statistical power to examine mortality from individual types of cancer and by survey. Pipe use was not assessed in the 2010 survey and had low prevalence in other survey years, which limited our ability to examine associations. Associations of cigar, pipe, and smokeless tobacco use with mortality for individual cancers, such as bladder cancer, should be interpreted with caution due to small numbers of deaths among users. We also lacked information about specific types of cigars and smokeless tobacco. Nevertheless, the nationally representative nature of our study means that participants used typical products available on the US market. Tobacco use was assessed at one time point, and therefore subsequent changes in tobacco usage patterns or tobacco products used by participants could have affected associations. We lacked information on age of cessation for cigar, pipe, and smokeless tobacco. Our study also lacked data on diet, physical activity, and other potential confounders. However, risk estimates for cigarette use and mortality have been little affected by adjustment for physical activity in previous analysis of the NHIS (17). Use of vaporizers, e-cigarettes, and other electronic nicotine delivery systems is growing in the United States; however, these products were not widely used at the time of the surveys included in our study. Finally, our risk estimates were for mortality outcomes and not for disease incidence or diseases that may not result in death.

In conclusion, this nationally representative US study provides additional evidence that exclusive use of cigarettes, cigars, and smokeless tobacco each increases the risk of mortality from

Table 4. Mortality from each smoking-related cancer by exclusive daily or nondaily use of cigarettes, cigars, or smokeless tobacco among current tobacco users with never tobacco users as a referent group: National Health Interview Survey 1991, 1992, 1998, 2000, 2005, and 2010

	Oral cavity	Esophagus	Stomach	Colon, rectum, and anus	Pancreas	Lung	Bladder
No. of deaths	108	179	148	772	493	2172	166
Never tobacco use, n	25	32	69	319	190	207	32
HR	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Cigarettes							
Former, No. of deaths	17	40	30	202	118	532	63
HR (95% CI)*	1.28 (0.65 to 2.53)	1.85 (0.91 to 3.74)	0.90 (0.55 to 1.47)	1.23 (0.96 to 1.57)	1.33 (1.01 to 1.74)	4.82 (3.87 to 5.99)	3.60 (2.16 to 5.98)
Current, all, No. of deaths	43	52	24	146	112	996	39
HR (95% CI)	5.32 (2.95 to 9.58)	3.26 (1.68 to 6.34)	1.57 (0.92 to 2.68)	1.68 (1.30 to 2.19)	2.29 (1.69 to 3.12)	15.49 (12.64 to 18.99)	4.48 (2.57 to 7.80)
Current, daily, No. of deaths	†	47	16	131	95	909	33
HR (95% CI)	6.23 (3.42 to 11.33)	3.60 (1.82 to 7.10)	1.24 (0.66 to 2.31)	1.72 (1.32 to 2.24)	2.29 (1.66 to 3.16)	16.77 (13.65 to 20.59)	4.60 (2.57 to 8.23)
Current, nondaily, No. of deaths	†	5	8	15	17	87	6
HR (95% CI)	1.20 (0.31 to 4.60)	1.58 (0.47 to 5.35)	3.06 (1.25 to 7.49)	1.50 (0.79 to 2.84)	2.34 (1.25 to 4.36)	8.73 (6.25 to 12.19)	3.84 (1.38 to 10.70)
Cigars							
Former, No. of deaths	0	†	†	6	†	†	0
HR (95% CI)	NA	2.33 (0.50 to 10.72)	1.87 (0.40 to 8.73)	0.83 (0.31 to 2.21)	0.94 (0.26 to 3.33)	0.63 (0.23 to 1.70)	NA
Current, all, No. of deaths	†	†	0	†	†	5	†
HR (95% CI)	1.77 (0.24 to 12.87)	0.56 (0.12 to 2.69)	NA	0.42 (0.10 to 1.79)	0.72 (0.10 to 5.27)	2.68 (0.95 to 7.51)	3.87 (0.50 to 29.74)
Current, daily, No. of deaths	0	0	0	†	0	†	†
HR (95% CI)	NA	NA	NA	0.79 (0.11 to 5.74)	NA	4.27 (0.92 to 19.75)	11.55 (1.47 to 90.60)
Current, nondaily, No. of deaths	†	†	0	†	†	†	0
HR (95% CI)	2.43 (0.33 to 17.66)	0.81 (0.17 to 3.87)	NA	0.24 (0.03 to 1.77)	1.13 (0.15 to 8.22)	1.86 (0.54 to 6.43)	NA
Smokeless tobacco‡							
Former, No. of deaths	†	†	†	5	0	†	0
HR (95% CI)	14.19 (1.94 to 103.73)	2.50 (0.54 to 11.54)	0.57 (0.08 to 4.20)	1.86 (0.69 to 5.06)	NA	0.47 (0.07 to 3.37)	NA
Current, all, No. of deaths	†	†	†	8	†	6	†
HR (95% CI)	8.81 (1.45 to 53.66)	1.29 (0.16 to 10.52)	0.92 (0.13 to 6.44)	1.27 (0.50 to 3.24)	1.55 (0.48 to 4.97)	2.68 (0.95 to 7.51)	6.56 (1.00 to 42.95)
Current, daily, No. of deaths	†	†	†	†	†	†	†
HR (95% CI)	9.89 (1.20 to 81.76)	1.73 (0.21 to 14.32)	1.19 (0.17 to 8.34)	1.29 (0.45 to 3.69)	0.53 (0.10 to 2.73)	1.39 (0.43 to 4.47)	8.44 (1.27 to 55.97)
Current, nondaily, No. of deaths	†	0	0	†	†	†	0
HR (95% CI)	6.06 (0.78 to 47.38)	NA	NA	1.22 (0.17 to 8.79)	5.35 (1.25 to 22.80)	6.04 (1.22 to 29.81)	NA

*Adjusted for sex, education level (<high school, high school, some college or associated degree, college, graduate or professional school, and missing), race or ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, non-Hispanic other, and missing), and survey year (1991, 1992, 1998, 2000, 2005, and 2010) using age at survey as the underlying time metric. Baseline hazards in the Cox models were stratified by 5-year birth cohort. CI = confidence interval; HR = hazard ratio; NA, not applicable.

†Values are suppressed for confidentiality of fewer than five individuals.

‡Chewing tobacco and snuff.

heart disease, cancer, and other causes and that quitting decreases risk. Because cigars and smokeless tobacco are commonly used in the United States, our results emphasize the importance of tobacco control policies that are aimed at these products in addition to cigarettes.

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