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Original Contribution

Association Between Reductions of Number of Cigarettes Smoked per Day and Mortality Among Older Adults in the United States

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Many smokers do not quit but instead reduce the number of cigarettes they smoke per day (CPD) over their lifetime. Yet the associations of such changes in CPD with health risks are unclear. We examined the association of changes in CPD with subsequent death in the period 2004–2011 among 253,947 participants of the National Institutes of Health–AARP Diet and Health Study. Using a questionnaire assessing responders' history of smoking cigarettes, we identified cigarette smokers who quit, decreased, maintained, or increased their CPD between ages 25–29 and 50–59 years. Hazard ratios and 95% confidence intervals were obtained from multivariable adjusted Cox proportional hazards regression models. Relative to never smokers, smokers who maintained a consistent CPD had 2.93 times (95% confidence interval (CI): 2.82, 3.05) higher all-cause mortality risk, and participants who increased their CPD had still higher risk (hazard ratio (HR) = 3.37, 95% CI: 3.23, 3.52). Death risk was lower among participants who decreased their CPD (HR = 2.38, 95% CI: 2.25, 2.52) or quit smoking (for quitting between ages 30 and 39 years, HR = 1.32, 95% CI: 1.25, 1.39). Similar patterns were observed for smoking-related causes of death, with particularly strong associations for lung cancer and respiratory disease. Reductions in CPD over the lifetime meaningfully decreased death risk; however, cessation provided a larger benefit than even large declines in CPD.

cigarette; lifetime change; mortality; prospective study; smoking

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; CPD, number of cigarettes smoked per day; ICD, *International Classification of Diseases*.

Tobacco products are estimated to cause 7 million premature deaths per year worldwide (1), including 480,000 deaths per year in the United States from cigarette smoking alone (2). According to many studies, the behaviors that lead to greater cumulative exposure to tobacco products, including younger age at initiation (3–6) and smoking more cigarettes per day (3, 4, 7, 8), increase risk for death and quitting lowers that risk (3, 7–9). The data are unambiguous: Nonsmokers should not start and smokers should quit.

Nevertheless, despite declines in prevalence, an estimated 15% of US adults smoke cigarettes (10), and 39% of US adults smoked cigarettes regularly at some point in their life (11). During their lifetime, many smokers do not quit smoking but instead make changes in their cigarette use, reducing or increasing the number

of cigarettes they smoke per day (CPD) over time (12–14). In recent years, a growing number of people who smoke cigarettes daily have reduced their CPD and some have become occasional smokers, rather than quitting. Surprisingly few data, however, are available on the possible health effects of such changes, despite the possibility that they may be substantial. According to data from 3 prior studies, reducing CPD may have some benefit for lung cancer risk (15–17), but associations with other endpoints, including overall mortality, have generally been null (17–23). However, these previous studies tended to be of modest size and changes in cigarette use were assessed over a relatively short time in them (15–17).

As part of the National Institutes of Health–AARP Diet and Health Study, more than 260,000 participants detailed their cigarette use at different age periods in their life. Using these data, we investigated the impact of changes in CPD on the risks of all-cause and cause-specific mortality.

METHODS

Study population

The National Institutes of Health-AARP cohort has been described previously (24). Briefly, between 1995 and 1996, 566,398 male and female participants from 6 US states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan) completed a questionnaire detailing tobacco use, diet, and lifestyle. Between 2004 and 2005, 313,363 participants (62.3%), aged 59-82 years, completed a follow-up questionnaire with detailed questions about cigarette smoking. We excluded proxies (n = 14,072), those who died before their questionnaires were scanned (n = 4), those with incomplete information about cigarette smoking (n = 9,295), those who reported ever cigarette smoking but not smoking during ages 25–29 years (n = 25,142), and those who reported smoking fewer than 100 cigarettes in their lifetime (n = 10,903), leaving 253,947 participants in our analysis. The cohort was approved by the Special Studies Institutional Review Board of the National Cancer Institute. Baseline questionnaires included a statement that participants provide informed consent by completing and returning the questionnaires.

Exposure assessment

As part of the 2004–2005 questionnaire, participants reported their cigarette smoking during 9 age periods (<15, 15–19, 20-24, 25-29, 30-39, 40-49, 50-59, 60-69, and 70 years or older), using the following 8 intensity categories for CPD: none, <1, 1-10, 11-20, 21-30, 31-40, 41-60, and ≥61). To assess changes in CPD, we classified participants who smoked cigarettes at ages 25-29 years (at which point most ever-smokers smoked cigarettes) by their later use at ages 50-59 years, as follows: participants who had quit (at ages 30-39, 40-49, or 50-59 years), participants who had maintained a consistent CPD during both age periods, those who reduced CPD but did not quit smoking cigarettes at ages 50-59 years, or participants who increased CPD at ages 50-59 years. Because some participants who completed the questionnaire were younger than 60 years, we did not include reported CPD at ages 60-69 years or 70 years or older in our analysis.

In the 2004–2005 questionnaire, participants also were asked about body mass index (computed using self-reported height and weight), physical activity, perceived general health, and history of certain health conditions. Information on age, sex, race or ethnicity, education, and 124 dietary items, including alcohol, was reported on the original 1995–1996 questionnaire.

Cohort follow-up and endpoints

Follow-up was from the date when the completed and returned 2004–2005 questionnaire was scanned until death or December 31, 2011, whichever came first. Participants were followed by linkage to the National Change of Address Index maintained by the National Center for Health Statistics. International Classification of Diseases (ICD)-9 and ICD-10 codes were used to define outcomes as follows: all cancer (ICD-9: 140–208, 238.6; ICD-10: C00–C97); lung cancer (ICD-9: 162.2–162.9; ICD-10: C34); heart disease (ICD-9: 390–398, 401–404, 410–429, 440–448; ICD-10: I00–I13, I20–I51, I70–I78); stroke (ICD-9: 430–438; ICD-10: I60–I69); and respiratory disease (e.g., pneumonia, influenza, chronic obstructive pulmonary disease (COPD), and allied conditions; ICD-9: 480–487, 490–496; ICD-10: J09–J18, J40–J47).

Statistical analysis

We computed death rates between ages 60 and 85 years by change in cigarette use from ages 25–29 to 50–59 years (i.e., quit, decreased, same, and increased) in men and women separately, with never smokers as the reference group. Hazard ratios and 95% confidence intervals were computed from Cox proportional hazards regression models (25) using personyears of follow-up as the underlying time metric. To adjust for birth-cohort effects, we stratified the baseline hazards by age groups (<65, 65–69, 70–74, ≥75 years) using the STRATA statement in the proc phreg procedure of SAS (SAS Institute, Inc., Cary, North Carolina) as we adjusted for age on a continuous scale. Other covariates in the final models included sex, level of education (high school or less, post-high school training, some college, completion of college), race or ethnicity (Non-Hispanic white, Non-Hispanic black, Hispanic, Asian, Pacific Islander, or Native American), alcohol intake (none, >0 to 1, >1 to 3, >3 drinks per day), and age at initiation of cigarette smoking. We did not adjust the final models for body mass index, perceived general health, and previous diagnosis of chronic diseases, because these factors are affected by cigarette use and also are associated with death. Adjustment for physical activity made little difference on the risk estimates (<2%), thus, those data were not included in the final models. We included variable-specific indicators for missing data in the regression models; less than 5% of the cohort lacked any single covariate. Our analyses were performed with SAS, version 9.3. All analyses were 2-sided and statistical significance was defined as P < 0.05.

We present subgroup analyses stratified by age group (i.e., <65, 65–69, 70–74, and \geq 75 years), sex, and by the first 5 or more years of follow-up. We also evaluated associations among participants who reported never regularly using pipes or cigars and among those who did not report a previous diagnosis of heart attack, stroke, COPD, or cancer. We investigated detailed changes in CPD from ages 25–29 to 50–59 years, with participants who reported smoking a consistent CPD during both age periods as the reference group. Finally, we evaluated changes in reported CPD between the 1995–1996 questionnaire and the later 2004–2005 questionnaire.

RESULTS

Of the cohort of 253,947 participants (mean age, 71 (range, 59–82) years) included in the analysis, 111,473 (56%) were

				Continue	ed to Smoke at Both Ag	e Periods
Category ^a	All Participants (n = 253,947), %	Never Smoker (n = 111,473), %	Guit Smoking by Ages 50–59 Years (n = 90,841), %	Smoked Less at Ages 50–59 Years (n = 10,466), %	No Change in CPD (n = 25,853), %	Smoked More at Ages 50–59 Years (<i>n</i> = 15,314), %
Age at start of follow-up, years ^{a,b}	71.1 (66.4, 75.1)	70.9 (66.3, 75.1)	70.7 (66.1, 74.9)	70.5 (65.8, 74.7)	72.1 (67.4, 75.7)	72.4 (67.9, 75.6)
Age started smoking, years ^a						
Never	43.9	100	0	0	0	0
<15	12.6	0	21.0	26.9	24.7	24.3
15–19	25.9	0	46.8	48.3	46.0	41.1
20–24	15.0	0	27.4	22.4	25.5	27.7
25–29	2.6	0	4.8	2.4	3.8	6.9
CPD at ages 25–29 years ^a						
None	43.9	100	0	0	0	0
<1–20 ^c	34.9	0	61.4	50.5	67.8	64.8
21–40	18.9	0	33.4	45.3	29.6	34.0
≥41 ^c	2.3	0	5.2	4.2	2.6	1.2
CPD at ages 50–59 years ^a						
None	79.7	100	100	0	0	0
<1–20 ^c	11.8	0	0	91.0	67.8	19.1
21–40	6.9	0	0	8.7	29.6	57.7
≥41 ^d	1.6	0	0	0.3	2.6	23.2
Male sex ^e	57.6	49.1	68.6	65.9	56.1	50.7
White race ^e	92.6	91.7	93.6	93.2	92.3	93.5
College education ^e	44.4	48.3	45.0	42.0	33.7	31.7
Body mass index ^{a,b,f}	26.5 (23.8, 29.6)	26.1 (23.6, 29.3)	26.6 (24.3, 29.9)	26.6 (23.9, 29.8)	26.2 (23.5, 29.3)	26.6 (23.8, 30.2)
Alcohol consumption >3 drinks/ day ^e	7.3	3.4	9.3	11.2	11.7	12.8
Leisure activity, MET-hours/ week ^{a,b}	14.9 (4.3, 36.6)	15.0 (4.3, 36.6)	18.8 (4.3, 40.8)	14.4 (4.2, 36.6)	10.8 (2.2, 29.5)	8.3 (1.1, 25.0)
Reported health (fair/poor) ^a	12.9	10.2	12.1	16.3	19.1	23.8

 Table 1.
 Characteristics Among All Participants and by Category of Cigarette Use Between the Ages 25–29 Years and 50–59 Years Assessed in the 2004–2005 Questionnaire of the National Institutes of Health–AARP Diet and Health Study

Table continues

			Outh Canadidate his Acco	Continue	ed to Smoke at Both A	ge Periods
Category ^a	All Participants (<i>n</i> = 253,947), %	Never Smoker (<i>n</i> = 111,473), %	duit annoking by Ages 50–59 Years (<i>n</i> = 90,841), %	Smoked Less at Ages 50–59 Years (<i>n</i> = 10,466), %	No Change in CPD (<i>n</i> = 25,853), %	Smoked More at Ages 50–59 Years (<i>n</i> = 15,314), %
Previous diagnosis ^a						
Heart attack	18.2	13.8	20.5	23.7	22.3	24.9
High blood pressure	53.9	51.4	55.7	55.3	54.7	58.1
High cholesterol level	55.3	51.5	57.3	59.1	57.1	59.1
Stroke	3.5	2.9	3.4	4.4	4.9	5.6
Chronic obstructive pulmonary disease	8.1	3.9	6.8	14.8	18.0	24.4
Cancer	26.9	25.2	27.9	28.4	28.3	29.6
Abbreviations: CPD, number of cig.	arettes smoked per day;	MET, metabolic equivaler	rt.			

Table 1. Continued

^a Assessed in 2004–2005.

^b Values are expressed as median (interquartile range)

 $^{\circ}$ Includes 2 categories (<1 CPD and 1–10 CPD) from the guestionnaire that were collapsed together.

Includes 2 categories (41–60 and >60 CPD) from the questionnaire that were collapsed together. ^e Assessed in 1995–1996

Weight (kg)/height (m)².

never smokers and 142,474 (44%) reported having smoked cigarettes at ages 25-29 years. A majority (69%) of smokers began smoking cigarettes when they were younger than 20 years. Of smokers at ages 25-29 years, 64% quit smoking cigarettes by ages 50-59 years, whereas 18% reported maintaining a consistent CPD, 7% smoked fewer cigarettes but did not quit, and 11% smoked more cigarettes.

Table 1 lists various aspects of participants' cigarette smoking history, including age at initiation, demographics, lifestyle, and health conditions overall and by category of cigarette use. Many demographic parameters, such as age, race, and body mass index, were similar across cigarette smoking categories. Participants who smoked a greater CPD at ages 50-59 years than at ages 25-29 years were less likely to have a college education, less physically active, and more likely to report higher alcohol consumption and fair or poor perceived general health, COPD, or a previous stroke than those who smoked fewer cigarettes at ages 50–59 years or those who had quit.

During a median follow-up of 7.1 years, 32,774 participants died: 12,195 of cancer (of whom 3,396 died of lung cancer), 8,328 of heart disease, 1,468 of stroke, 2,784 of respiratory disease, and 7,999 of other causes. The death rate was lowest among never smokers and progressively increased among former smokers, those who had reduced their CPD but did not quit, those who maintained a consistent CPD, and those who had increased their CPD from ages 25-29 to 50-59 years (Figure 1). Death rates at ages 80–85 years were 3,380 per 100,000 among never smokers, and 4,542, 5,949, 7,260, and 7,870 per 100,000 among cigarette smokers who quit, decreased the CPD but did not quit, maintained their CPD, and increased CPD, respectively, in men and 2,986, 3,975, 5,440, and 5,984 per 100,000, respectively, in women.

Relative to never smokers, all-cause mortality risk among participants who maintained a consistent CPD at ages 25-29 and 50-59 years was 2.93 times higher (95% confidence interval (CI): 2.82, 3.05), whereas the risk was still higher among participants who had increased their CPD (hazard ratio = 3.37, 95% CI: 3.23, 3.52; Table 2). Participants who had decreased their CPD but had not quit had 2.38 times higher risk (95% CI: 2.25, 2.52) than never smokers; however, death risk was substantially lower among participants who had quit smoking, with the lowest risks observed among those who had quit at ages 30-39 years (hazard ratio = 1.32, 95% CI: 1.25, 1.39). Adjusting for previous diagnoses of chronic disease (e.g., heart attack, high blood pressure, high cholesterol level, stroke, COPD, and cancer) did not change the association (data not shown).

In age-stratified analysis, associations were strongest among participants younger than 65 years at baseline and modestly attenuated with older age (P for interaction < 0.0001) (Web Table 1). Relative to never smokers, the hazard ratios were 3.10 (95% CI: 2.62, 3.66), 3.56 (95% CI: 3.10, 4.09), and 4.70 (95% CI: 4.03, 5.47) for smokers who had decreased CPD, maintained a consistent CPD, or increased CPD among participants younger than 65 years, with corresponding hazard ratios of 2.07 (95% CI: 1.89, 2.27), 2.57 (95% CI: 2.41, 2.73), and 2.90 (95% CI: 2.70, 3.11) for these same respective comparisons among participants who were 75 years or older. Associations were slightly stronger in women than in men (P for interaction = 0.009). For example, relative to never smokers, the hazard ratios for those who increased CPD were 3.83 (95% CI: 3.54, 4.14) in women and



Figure 1. Death rate per 100,000 people from ages 60 to 85 years by prior change in cigarette use from ages 25–29 to 50–59 years reported in the 2004–2005 questionnaire among (A) men and (B) women in the National Institutes of Health–AARP Diet and Health Study.

3.19 (95% CI: 3.02, 3.37) in men, and the hazard ratios for those who decreased CPD but did not quit were 2.79 (95% CI: 2.51, 3.10) for women and 2.25 (95% CI: 2.11, 2.40) for men. Comparable associations were observed for deaths occurring in the first 5 years or later in follow-up, after excluding participants who reported ever regularly using pipes or cigars on the 1995–1996 questionnaire, and after excluding participants who reported 1 or more previous diagnoses of heart attack, stroke, COPD, or cancer.

Consistent patterns were observed for deaths due to a range of smoking-related diseases, with especially strong associations observed for deaths resulting from lung cancer and respiratory disease (Table 2). Hazard ratios for decreasing, consistent, and increasing CPD from ages 25–29 to 50–59 years relative to never smokers for all cancers were, respectively, 2.37, 3.26, and 3.53; for lung cancer, 13.47, 21.75, and 27.16; for heart disease, 2.12, , 2.46, and 2.84; for stroke, 1.68, 1.95, and 2.19, and for respiratory disease, 11.42, 15.66, and 20.31.

We analyzed whether more granular changes in CPD between the ages of 25-29 and 50-59 years were associated with death risk, using participants who maintained a consistent CPD as the reference group (Table 3). We observed evidence for a dose response across increasing categories of reported use (P for trend < 0.0001), with larger changes in CPD associated with larger changes in risk for death. For example, relative to smokers whose CPD consistently ranged from more than 0 to 10 at both age periods, the hazard ratios for those who increased to 11-20, 21-30, and >30 CPD were 1.39 (95% CI: 1.25, 1.55), 1.47 (95% CI: 1.23, 1.75), and 1.82 (95% CI: 1.47, 2.24), respectively, whereas the hazard ratio for those who had quit was 0.70 (95% CI: 0.65, 0.76). Conversely, relative to those whose CPD was consistently more than 30, the hazard ratios for reducing to 21-30, 11-20, and from more than 0 to 10 CPD were 0.85 (95% CI: 0.73, 0.99), 0.76 (95% CI: 0.63, 0.91), and 0.64 (95% CI: 0.51, 0.80), with a hazard ratio for quitting of 0.51 (95% CI: 0.48, 0.55).

The aforementioned analyses relied on participants recalling their historical cigarette use. Such recall may be affected by misclassification; thus, we examined whether changes in CPD between the 1995–1996 questionnaire and the later 2004–2005 questionnaire were associated with subsequent death risks. Although this analysis was restricted to current smokers in 1995–1996 (n = 141,084), and as such had lower statistical power than our main analyses, results were concordant with those from the larger cohort (Web Table 2).

DISCUSSION

According to our data, the association of smoking with death appears to be dynamic and sensitive to changes in CPD over the lifetime. Larger decreases in CPD from ages 25–29 to 50–59 years were associated with lower death risks than were smaller decreases in CPD. Conversely, larger increases in CPD were associated with higher death risks than were smaller increases in CPD. Nevertheless, death rates were substantially lower among former smokers than among participants who had reduced their CPD but continued to smoke.

Associations between death and age at smoking initiation (3-6), age at smoking cessation (3, 7-9), and CPD (3, 4, 7, 8)have been demonstrated in several studies. To our knowledge, however, changes in CPD during the lifetime that affect death risk have been examined in just 4 studies. Compared with those who smoked a consistent CPD, hazard ratios for reducing CPD were 1.04 (95% CI: 0.95, 1.14) (21), 1.02 (95% CI: 0.89, 1.17) (19), 1.02 (95% CI: 0.84, 1.22) (17), and 0.85 (95% CI: 0.77, (0.95) in these prior studies (18). Of the 2 prior studies in which increasing CPD was investigated, death risk estimates were 1.14 (95% CI: 0.99, 1.32) (18) and 1.16 (95% CI: 1.06, 1.28) (21) relative to those smoking a consistent CPD. In 3 prior studies (15-17), including the largest to date (16), evidence was found for lower risk of lung cancer in participants who reduced their CPD. Results for other outcomes were generally null (17-23). However, these studies tended to be smaller and to assess changes in cigarette use over a shorter time than in the current study. In the current study, we assessed changes in CPD over decades, whereas prior studies assessed changes over a shorter time (from 2 years (18) to a maximum of 3–13 years (17)). Although results from the previous studies are not completely

Cigorotto Smoking			All Cause	S		All Cance	ers		Lung Ca	ncer
Status	No.	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% Cl	No. of Deaths	HRª	95% CI
Never smoker	111,473	9,821	1.00	Reference	3,468	1.00	Reference	253	1.00	Reference
Age period quit smoking, years										
30–39	21,397	2,075	1.32	1.25, 1.39	795	1.38	1.27, 1.51	119	3.07	2.45, 3.86
40–49	35,202	4,203	1.52	1.45, 1.59	1,595	1.60	1.49, 1.72	326	4.86	4.07, 5.80
50–59	34,242	5,082	1.93	1.85, 2.01	1,913	2.03	1.89, 2.17	594	9.17	7.81, 10.77
Continued to smoke at ages 50–59 years										
Smoked less	10,466	1,926	2.38	2.25, 2.52	662	2.37	2.16, 2.59	260	13.47	11.21, 16.20
Smoked the same amount	25,853	5,855	2.93	2.82, 3.05	2,308	3.26	3.05, 3.47	1,069	21.75	18.71, 25.27
Smoked more	15,314	3,912	3.37	3.23, 3.52	1,454	3.53	3.29, 3.80	775	27.16	23.27, 31.71
P for trend ^b			<	<0.0001		<	0.0001			<0.0001
	-	He	eart Dise	ase		Stroke	9	Res	piratory	Disease
	-	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI
Never smoker	111,473	2,631	1.00	Reference	550	1.00	Reference	324	1.00	Reference
Age period quit smoking, years										
30–39	21,397	520	1.17	1.05, 1.31	103	1.33	1.04, 1.71	90	2.34	1.83, 2.99
40–49	35,202	1,087	1.38	1.26, 1.50	199	1.43	1.16, 1.76	216	3.12	2.59, 3.77
50–59	34,242	1,346	1.81	1.67, 1.97	208	1.56	1.27, 1.91	409	6.02	5.12, 7.08
Continued to smoke at age 50–59 years										
Smoked less	10,466	455	2.12	1.90, 2.37	64	1.68	1.26, 2.23	225	11.42	9.50, 13.71
Smoked the same amount	25,853	1,377	2.46	2.27, 2.67	206	1.95	1.60, 2.38	858	15.66	13.55, 18.09
Smoked more	15,314	912	2.84	2.60, 3.10	138	2.19	1.76, 2.74	662	20.31	17.50, 23.57
P for trend ^b			<	<0.0001		<	0.0001		-	<0.0001

 Table 2.
 Association Between Change in Cigarette Use Between Ages 25–29 Years and 50–59 Years Reported on the 2004–2005

 Questionnaire and Subsequent All-Cause and Cause-Specific Mortality in the National Institutes of Health–AARP Diet and Health Study

Abbreviations: CI, confidence interval; HR, hazard ratio.

^a From Cox proportional regression adjusted for age, sex, education, race or ethnicity, alcohol intake, and age at smoking initiation, stratified by age group (<65, 65–69, 70–74, or \geq 75 years) using the STRATA statement in SAS, version 9.3. Never smokers served as the reference group.

 $^{b}\chi^{2}$ test for linear trend across increasing categories, with never smokers as the reference group.

consistent, our results are plausible. In many previous studies, dose-dependent associations with CPD and lifetime exposure metrics, such as pack-years, have been demonstrated with disease endpoints and mortality (2). Lower death risks among people who quit smoking than those who did not quit but instead reduced their CPD to fewer than 10 are also plausible and consistent with recent findings from the National Institutes of Health–AARP cohort that smokers whose CPD was consistently fewer than 1 and was 1–10 CPD over their lifetime have higher death risks than never smokers and benefit from cessation (12).

Key strengths of our study include its very large size, prospective design, and detailed assessment of cigarette smoking over the lifespan. One advantage of the prior studies is that the authors independently assessed smoking at 2 time points as opposed to asking participants to recall their history of smoking history over their lifetime, as in the current study. Although such recall may lead to misclassification, self-reported smoking has been shown to have good correlation with biomarkers, such as nicotine and its metabolites, in blood and urine (26, 27). Recalling previous smoking history has good validity for CPD 20 years earlier ($\kappa =$ 0.63) and fair validity for CPD 32 years earlier ($\kappa =$ 0.36) in middle-aged adults (28). In the National Institutes of Health– AARP cohort, we showed that 74% of participants who reported on the 2004–2005 questionnaire that they consistently smoked 10 or fewer cigarettes daily reported smoking a consistent CPD on the 1995–1996 questionnaire (12). We also observed comparable findings in a sensitivity analysis in which we defined changes in CPD across 2 separate study questionnaires

							5	CPD at Ages	25–29 Year	Ş						
CPD at Ages 50–59			10 ^a			11-2	0			21-6	l			>3(<u>م</u>	
Years	No.	No. of Deaths	нR°	95% CI	No.	No. of Deaths	нR°	95% CI	No.	No. of Deaths	НR ^c	95% CI	No.	No. of Deaths	нR°	95% CI
None	23,131	2,338	0.70	0.65, 0.76	32,660	4,049	0.57	0.54, 0.59	19,776	2,640	0.50	0.47, 0.53	15,274	2,333	0.51	0.48, 0.55
<1-10	6,856	666	1.00	Referent	4,263	689	0.80	0.74, 0.87	1,201	188	0.64	0.55, 0.74	436	79	0.64	0.51, 0.80
11–20	2,645	505	1.39	1.25, 1.55	11,996	2,597	1.00	Referent	2,021	394	0.74	0.66, 0.82	575	123	0.76	0.63, 0.91
21–30	694	143	1.47	1.23, 1.75	3,560	862	1.17	1.08, 1.26	5,287	1,438	1.00	Referent	766	189	0.85	0.73, 0.99
≥31	368	97	1.82	1.47, 2.24	2,362	645	1.23	1.12, 1.34	3,835	1,124	1.06	0.98, 1.15	4,768	1,521	1.00	Referent
P for trend ^d			v ∼	0.0001			V	J.0001			V	D.0001			Ŷ	0.0001

Association Between Changes in Cigarette Use Between Ages 25–29 Years and 50–59 Years Reported in the 2004–2005 Questionnaire and Subsequent All-Cause Mortality in the

Fable 3.

^a Includes 2 categories (<1 and 1–10 cigarettes per day) from the questionnaire that were collapsed together.

Includes 3 categories (31–40, 41–60, and >60 cigarettes per day) from the questionnaire that were collapsed together.

^o From Cox proportional hazard regression adjusted for age, sex, education, race or ethnicity, alcohol intake, and age at smoking initiation, stratified by age group (<65, 65–69, 70–74, or \geq 75 group comprised those participants who reported smoking a consistent amount of cigarettes at both age periods $^{
m d}$ χ^2 test for linear trend across increasing categories, with former smokers at age 50–59 years as a reference group. years) using the STRATA statement in SAS, version 9.3. Reference

administered 8–10 years apart, which provides reassurance with regard to our main findings.

A general limitation of studies to date is a lack of information on participants' motivation for changing their CPD. One possibility is poor health, which likely would have led to a smoking reduction rather than the reverse. However, similar associations were observed after excluding participants who reported a previous chronic disease diagnosis, or after excluding deaths that occurred during the first 5 years of follow-up in the current study, even though such exclusions preferentially affected heavy smokers in the cohort. Also, we observed that participants who had reduced their CPD subsequently reported better health and less COPD than participants who had maintained a consistent CPD. These data support the observed association between reducing CPD and lower death risk.

Because participants in our analysis had a median age of 71 years and a minimum age of 59 years, we were unable to assess risks in younger adults. Heavy smokers were less likely to have lived long enough to enter our study than lighter and former smokers (14, 29). Therefore, one might predict that our study underestimates the impact of cigarette smoking on death and may underestimate the magnitude of associations with quitting smoking and reducing CPD over the lifetime. Our study represents a specific point in time: birth cohorts who began cigarette smoking in the 1940s and 1950s and began to quit in large numbers after the publication of the 1964 Surgeon General's report (14, 30). Our study participants were also predominantly non-Hispanic whites. Studies in younger populations, in other birth cohorts, and in racial or ethnic minority populations are clearly needed. We lacked assessment of inhalation, and this and other aspects of smoking topography may change over the lifetime. For example, to satisfy their craving for nicotine, participants who reduced their CPD may compensate by smoking each remaining cigarette more intensely (22, 31). Nevertheless, according to the current findings, any compensatory effects are secondary to the larger effects of increasing or reducing CPD. Last, as in all observational studies, residual confounding by measured and unmeasured factors are possible.

Based on the time point and age distribution of the cohort, we can assume that most participants altered their cigarette use in the absence of nicotine replacement therapy, e-cigarettes, or other nicotine delivery devices. Nevertheless, partial substitution of cigarettes with other tobacco products may have health benefits, according to our data, should the other products be less harmful than cigarettes. However, studies are needed to directly evaluate the health risks of low CPD in combination with other tobacco products, particularly because dual use of cigarettes and other tobacco products is increasingly common.

In addition to providing important information for public health, our results may also have implications for risk prediction. For example, eligibility for lung cancer screening is typically determined on the basis of lifetime pack-years of exposure, the product of cigarette-smoking duration and typical or recent CPD (32). Yet, we found the hazard ratios for lung cancer deaths varied substantially by changes in CPD over the lifetime. Therefore, models that incorporate CPD at just a single time in life may not optimally identify people who should be screened for lung cancer. Studies are needed to evaluate the impact of changing CPD over the lifetime on the effectiveness of lung cancer screening. In conclusion, among older Americans in a large, prospective cohort study, participants who increased CPD over their lifetime had higher death rates, whereas participants who reduced CPD but did not quit had lower death rates, although these were substantially higher than for participants who quit smoking. According to our data, never smoking cigarettes is best, and cessation provides the greatest benefit for current cigarette smokers. Nevertheless, reducing CPD was associated with lower death rates.

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