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Association of Cigarette Smoking From Adolescence to Middle-Age With Later Total and Cardiovascular Disease Mortality

The Harvard Alumni Health Study

To the Editor: Evidence regarding the future health impact of smoking at younger ages is usually based on retrospective reporting of this health behavior, which demonstrates only moderate agreement with contemporaneous reporting (1). Studies of subsequent mortality risk with prospectively measured smoking in adolescence or early adulthood are rare and tend to focus on total mortality (2,3). Only one study (4) has considered cause-specific mortality, in particular cardiovascular disease (CVD). In addition, the single baseline measure of smoking in adolescence used in these studies is unlikely to completely capture lifetime risk. For example, there is evidence that mortality risk in lifelong smokers versus lifelong nonsmokers is far greater than that estimated for current smokers versus nonsmokers at any individual time point (2).

Cigarette smoking in adolescence is common and continues to increase. Policy makers require reliable estimates of risk disease burden. Accordingly, we have explored all-cause, CVD, and cancer mortality associations with cigarette smoking in early adulthood to older age in a large cohort of male U.S. college students. To our knowledge, this duration of lifetime prospective measurement of cigarette smoking is unrivaled in the literature.

The Harvard Alumni Health Study is an ongoing cohort study of male alumni from Harvard University who entered college between 1916 and 1950. Cigarette smoking status was obtained at baseline during a medical examination, and comparable smoking data were also reported in follow-up surveys in 1962/1966, 1977, and 1988. We explored baseline smoking associations with mortality to the end of 1998 from: 1) all causes, 2) CVD, 3) cancers related to smoking, and 4) cancers not related to smoking, using Cox proportional hazards regression. We also examined the associations of all-cause mortality with continuing smoking status based on smoking status collected at baseline and in 1962/1966, 1977, and 1988. Men were defined as continuing nonsmokers (nonsmoker at all 4 time points), continuing smokers (current smokers at all 4 time points), or quitters (current smoker at baseline and nonsmoker by 1988 with only 1 change in status). Men who changed their smoking status more than once or took up smoking during follow-up were omitted from these analyses. There were too few deaths to explore cause-specific mortality in this context.

Of 33,415 men in the original cohort, 28,236 (84.5%) had data on cigarette smoking at baseline (mean age 18 years). Baseline characteristics of men included and excluded from analyses were similar. Overall, 10,253 men (36.3%) smoked at baseline, although the proportion of smokers varied according to the decade of interview: Approximately one-quarter of men interviewed in the 1910s were

cigarette smokers, and this proportion increased steadily to 40.6% in the 1940s before decreasing to 34.3% in the 1950s. After a median follow-up period of 53.2 (range: 0.3 to 83.5) years, 13,704 men (48.5%) had died. Men reporting that they smoked cigarettes at baseline experienced a 30% (95% confidence interval [CI]: 26% to 35%) increase in mortality from all causes (Table 1) compared with those who were nonsmokers. Mortality for specific causes was also increased in men who were smokers at baseline. As anticipated, this was most marked for smoking-related cancers (hazard ratio [HR]: 1.91; 95% CI: 1.72 to 2.12), and there was also a clear 20% (14% to 27%) increase in CVD mortality in men who smoked in early adulthood.

Analysis of continuing smoking status was based on 5,785 men with complete data on smoking at baseline, 1962/1966 (mean age 42 years), 1977 (mean age 55 years), and 1988 (mean age 66 years). At baseline, 2,269 (39.2%) of these men were cigarette smokers, and the impact of smoking was similar to that in the full cohort. Among baseline smokers, 1,303 (57.4%) were still smoking in 1966, 573 (25.3%) were still smoking in 1977, and only 253 (11.1%) were continuing smokers in 1988. Mortality in continuing smokers was more than double that in continuing nonsmokers (HR: 2.11; 95% CI: 1.63 to 2.74), while mortality in men who smoked at baseline but subsequently quit was higher than in continuing nonsmokers but markedly lower than in those who continued to smoke (HR: 1.29; 95% CI: 1.15 to 1.46).

The negative health effects of cigarette smoking are well understood, yet smoking rates in young people are continuing to rise. The link between adolescent smoking and later mortality has been little examined, particularly in the context of CVD mortality. Although adolescent smoking patterns in our cohort may differ from those of contemporary adolescents, our results indicate that cigarette smoking reported directly in early adulthood has a negative impact on mortality, particularly due to CVD and smoking-related cancers, more than 50 years later. Although exposure prevalence may differ, there is every reason to anticipate that these smoking-mortality results have contemporary relevance and they are consistent with other evidence (2–4). Changing smoking rates by baseline year track the increasing popularity of cigarette smoking during the first half of the 20th century, followed by a decline in uptake as negative health effects became more widely understood in the 1960s. It is interesting that almost 90% of baseline smokers had quit by 1988, reflecting increasing public health information during this period. The beneficial effects of quitting smoking, as seen previously (5), are clear, with the excess mortality reduced in

Table 1 Hazard Ratio (95% Confidence Interval) for Mortality in Relation to Baseline and Continuing Smoking Status (The Harvard Alumni Health Study)

	Men With Baseline Smoking Data (N = 28,236)		Men With Continuing Smoking Data (N = 5,785)	
	N (Alive/Died)	HR* (95% CI)	N (Alive/Died)	HR* (95% CI)
All cause				
Baseline smoking				
Nonsmoker	9,419/8,564	1.00 (ref)	2,782/734	1.00 (ref)
Cigarette smoker	5,113/5,140	1.30 (1.26–1.35)	1,767/502	1.36 (1.21–1.52)
p Value		<0.001		<0.001
Continuing smoking†				
Continuing nonsmoker			2,782/734	1.00 (ref)
Continuing smoker			190/63	2.11 (1.63–2.74)
Quit during follow-up			1,577/439	1.29 (1.15–1.46)
p Value				<0.001
CVD‡				
Baseline smoking				
Nonsmoker	14,290/3,693	1.00 (ref)		
Cigarette smoker	8,287/1,966	1.20 (1.14–1.27)		
p Value		<0.001		
Smoking-related cancer‡,§				
Baseline smoking				
Nonsmoker	17,222/761	1.00 (ref)		
Cigarette smoker	9,562/691	1.91 (1.72–2.12)		
p Value		<0.001		
Nonsmoking-related cancer‡,§				
Baseline smoking				
Nonsmoker	16,750/1,233	1.00 (ref)		
Cigarette smoker	9,617/636	1.10 (1.00–1.21)		
p Value		0.06		

*Adjusted for age at baseline examination and year of baseline examination; additional adjustments for height, body mass index, blood pressure, exercise, alcohol at baseline, and socioeconomic status in 1988 had little impact on these associations. †Based on smoking at: 1) baseline, 2) 1962/1966, 3) 1977, and 4) 1988. ‡There were too few deaths to explore associations with continuing smoking habits for this cause. §Cancers considered to be related to smoking were lung, oral cavity, nasopharynx, oropharynx, hypopharynx, nasal cavity and paranasal sinuses, larynx, esophagus, stomach, pancreas, liver, kidney (body and pelvis), ureter, urinary bladder, uterine cervix, and myeloid leukemia; all other cancers were considered not to be related to smoking.

CI = confidence interval; CVD = cardiovascular disease; HR = hazard ratio.

those who quit in comparison with those who continued to smoke. Health education should be targeted at preventing smoking uptake in young people and encouraging current smokers to quit.

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