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Smoking Reduction, Smoking Cessation, and Mortality: A 16-year Follow-up of 19,732 Men and Women from the Copenhagen Centre for Prospective Population Studies

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The authors investigated the association between changes in smoking habits and mortality by pooling data from three large cohort studies conducted in Copenhagen, Denmark. The study included a total of 19,732 persons who had been examined between 1967 and 1988, with reexaminations at 5- to 10-year intervals and a mean follow-up of 15.5 years. Date of death and cause of death were obtained by record linkage with nationwide registers. By means of Cox proportional hazards models, heavy smokers (≥15 cigarettes/day) who reduced their daily tobacco intake by at least 50% without quitting between the first two examinations and participants who quit smoking were compared with persons who continued to smoke heavily. After exclusion of deaths occurring in the first 2 years of follow-up, the authors found the following adjusted hazard ratios for subjects who reduced their smoking: for cardiovascular diseases, hazard ratio (HR) = 1.01 (95% confidence interval (CI): 0.76, 1.35); for respiratory diseases, HR = 1.20 (95% CI: 0.70, 2.07); for tobacco-related cancers, HR = 0.91 (95% CI: 0.63, 1.31); and for all-cause mortality, HR = 1.02 (95% CI: 0.89, 1.17). In subjects who stopped smoking, most estimates were significantly lower than the heavy smokers'. These results suggest that smoking reduction is not associated with a decrease in mortality from tobacco-related diseases. The data confirm that smoking cessation reduces mortality risk.

mortality; smoking; smoking cessation

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

The health benefits derived from quitting smoking are considerable and well-documented over a wide spectrum, including society-based economic calculations and assessments of increase in individual life expectancy (1). Nevertheless, efforts to diminish the harmful effects of tobacco use by preventing initiation of the habit and encouraging smoking cessation have had limited success (2). Stagnation of the decrease in smoking prevalence in developed countries, together with increased smoking initiation among adolescents, indicates that the health consequences of smoking will remain a profound challenge for health professionals in the 21st century (3). Consequently, alternative strategies for "harm reduction" are emerging. One such noncessation approach, one that has attracted much attention, is "smoking reduction," meaning a reduction in the number of cigarettes smoked per day among continuing smokers. It has been suggested that smoking reduction could be accepted as a goal in itself among heavy smokers who are unable or unwilling to quit completely (4–11). However, this method is not evidence-based (12), and a number of concerns have been raised, such as the ability of smokers to reduce and maintain a potential reduction, the extent of compensational smoking, the risk of undermining smoking cessation efforts, and whether smoking reduction in fact leads to a decreased risk of smoking-related diseases (12, 13). Studies have shown that a substantial proportion of smokers are capable of reducing their daily number of cigarettes and of maintaining this reduction (14–21). However, it

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TABLE 1. Overview of the study population obtained by combining three cohorts (n = 19,732), Copenhagen Centre for Prospective Population Studies, Copenhagen, Denmark, 1967–1988

Cohort of origin	Years of examinations*	No. of men	No. of women
Copenhagen City Heart Study	1976/1983	4,775	6,212
Glostrup Population Studies, 1897 cohort	1967/1977	84	112
Glostrup Population Studies, 1914 cohort	1974/1984	342	296
Glostrup Population Studies, 1936 cohort	1976/1981	456	500
MONICA I †	1981/1988	1,499	1,453
Copenhagen Male Study	1970/1976	4,003	
Total	1967/1988	11,159	8,573

* Years of the first and second examinations, respectively.

† The MONICA Project (Monitoring of Trends and Determinants in Cardiovascular Disease) is an international study conducted by the World Health Organization to monitor trends in and determinants of mortality from cardiovascular disease.

is still unclear from these studies whether subsequent cessation is facilitated or undermined, and the health consequences of smoking reduction have not been examined.

The aim of this investigation, based on data from three longitudinal studies conducted in the Copenhagen area, was to determine whether a reduction of at least 50 percent in the daily amount of tobacco smoked was associated with decreases in all-cause mortality and mortality from cardiovascular disease, tobacco-related cancers, and respiratory disease (chronic obstructive pulmonary disease and pneumonia) in comparison with people who continued to smoke at the same level. We also analyzed mortality risk among participants who stopped smoking during the study period.

MATERIALS AND METHODS

Study population

The Copenhagen Centre for Prospective Population Studies coordinates data from three comprehensive Danish population studies conducted in and around Copenhagen, Denmark: the Copenhagen City Heart Study, the Glostrup Population Studies (now being hosted by the Copenhagen County Centre of Preventive Medicine), and the Copenhagen Male Study. All of these studies have been described in detail previously (22–24). Briefly, the Copenhagen City Heart Study comprised 18,039 persons and the Glostrup Population Studies (including the MONICA I Project) comprised 9,991 persons from three birth cohorts. Both study populations were age-stratified and randomly selected from defined areas in Greater Copenhagen. The Copenhagen Male Study consisted of 5,241 men from 14 large workplaces in Copenhagen. All examinations included a self-administered questionnaire containing questions related to health and lifestyle, as well as a detailed physical examination. The mean response rate was 77 percent (range, 69–88 percent). The present analysis comprised 19,732 participants: 11,159 men and 8,573 women who provided adequate information on smoking habits at two examinations approximately 5 years apart. For the Copenhagen City Heart Study, data from examinations conducted in 1976/1978 and 1981/1983 were used (Copenhagen City Heart Studies I and II). For the Glostrup Population Studies, we used data from examinations that took place between 1967 and 1983 and corresponding follow-ups carried out between 1977 and 1988. Participants from the Copenhagen Male Study were examined on three occasions between 1970 and 1985, and for this cohort we used data from the first (1970–1971) and second (1976–1977) examinations. An overview of data on the pooled cohorts is given in table 1.

Follow-up

At the second examination, smoking habits and covariates were reassessed, thus defining the baseline point and the beginning of follow-up from this point onwards. Participants were followed until September 27, 2000, for all-cause mortality by record linkage with the Central Population Register and until December 31, 1997, for cause-specific mortality by record linkage with the Central Death Register. The mean duration of follow-up was 15.5 years. The only possible means of loss to follow-up was emigration, which was less than 0.5 percent.

For deceased participants, the cause of death was obtained from official death certificates kept at the National Board of Health. Deaths were coded according to the Eighth and Tenth revisions of the *International Classification of Diseases* (cardiovascular diseases: codes 390–458 and I00–I99; tobacco-related cancers: cancers of the respiratory tract, including lung cancer (codes 160–163, C32–C34, and C39), and cancers of the upper digestive tract (codes 140–141, 143–150, C00–C06, and C09–C15), including cancer of the pancreas (codes 157 and C25), kidney (codes 189 and C64), and urinary bladder (codes 188 and C67); respiratory diseases: chronic obstructive pulmonary disease (codes 490–

492 and J40–J44) and pneumonia (codes 480–486 and J12–J18)).

Assessment of smoking and smoking reduction

Smoking status and changes in smoking habits were based on self-report. At each examination, subjects were asked whether or not they smoked and, if the answer was affirmative, about the amount smoked (in absolute numbers), duration, inhalation, and preferred type of tobacco (cigarettes, cigars, cheroots, pipes, and mixed types). Ex-smokers were asked about duration of smoking and time since quitting. Total tobacco consumption expressed in grams per day was calculated by equating a cigarette to 1 g of tobacco, a cheroot to 3 g, and a cigar to 5 g.

The definition of smoking reduction was derived mainly from clinical studies of heavy smokers who reduce their smoking, in which (preferably) a 50 percent reduction or more in the amount smoked is achieved (4, 25). Thus, to measure a substantial reduction in tobacco consumption, we defined smoking reduction as having reported smoking ≥15 g of tobacco per day at the first examination and having subsequently reported at the second examination a decrease of at least 50 percent without quitting. This implies, for instance, that a participant who reported smoking 40 cigarettes per day at the first examination and 15 cigarettes per day at the second examination would be considered a "reducer," whereas he would be considered a continuous heavy smoker if he reported smoking 25 cigarettes per day at the second examination. Sustained ex-smoking was defined as reporting being an ex-smoker at both examinations, whereas new ex-smokers were subjects who reported active smoking at the first examination and no smoking at the second examination. The study population was then divided into the following categories: reducers, sustained never smokers, sustained ex-smokers, new ex-smokers (quitters), sustained light smokers (1–14 g/day), and sustained heavy smokers (≥15 g/day).

Statistical analysis

For comparison of proportions and mean values, the chi-squared statistic with two-tailed p values and the t test were applied. Age-adjusted mortality rates were calculated for men and women using the method of direct standardization and weighting equal to the total distribution of person-years over age groups. Cox proportional hazards regression models (26) were used to calculate the hazard ratios (relative risks) associated with all-cause and cause-specific mortality. The primary variable of interest was the grouping of subjects into six smoking categories as described above, with sustained heavy smokers constituting the reference group. Age was chosen as the underlying time scale, with age at the second examination used as the study baseline age. In the multivariable model, the following covariates were included: sex, cohort of origin, body mass index (weight (kg)/height $(m)^2$) in four categories (<20, 20–24, 25–29, ≥30), educational level in three categories (≤7 years, 8–11 years, ≥12 years), duration of smoking (continuous), and inhalation (yes/no). To allow for a possible "diagnostic" bias, meaning that some individuals might quit or reduce their smoking due to preexisting illness or symptoms, all analyses excluded events that occurred up to 2 years after the beginning of follow-up. Possible residual confounding by different inhalation habits with type of tobacco smoked was taken into account by stratifying analyses according to type of tobacco smoked (cigarette smokers versus smokers of cigars, cheroots, or pipes). Because there were too few cause-specific events among noncigarette smokers, this analysis was restricted to all-cause mortality.

The adequacy of the model was checked by testing the proportional hazards assumption in different ways: by conducting the standard graphic check based on the log of the cumulative hazard; by adding an interaction term between our primary independent variable of interest and a proxy variable for a subject's mean time in the study; and by performing a formal test of proportionality based on Schoenfeld residuals according to the method of Hosmer and Lemeshow (27). All three methods revealed that there were nonproportional hazards between the smoking groups and that a more complicated model-building strategy was necessary. The testing of the proportional hazards assumption showed that the violation of this assumption concerned the nonproportional hazards between never smokers and sustained ex-smokers on the one hand and the other smoking groups on the other. By dividing the study population into two groups (never and ex-smokers vs. reducers, quitters, and continuous smokers) and stratifying the analyses on this new dichotomous covariate, we developed a model that allowed for different baseline hazards in the two strata but assumed the same effect of other covariates in the model. This made it possible to compare the smoking groups within strata using simple hazard ratios but not between strata (for example, never smokers and reducers). Within these defined strata, the proportional hazards assumption was verified. All results of the survival analyses are presented as hazard ratios and 95 percent confidence intervals. The analyses were performed using the Stata statistical software package (28).

RESULTS

Table 2 shows the distribution of baseline characteristics and confounders for the six smoking strata. The 858 reducers (10 percent of the original smokers of ≥15 g/day) were significantly more likely to be male, to be older, to have been smoking for a longer period of time, to smoke other types of tobacco besides cigarettes, and to inhale less in comparison with continuous heavy smokers. The reducers reduced their tobacco consumption from a mean of 22.5 g/day at the first examination to a mean of 8.5 g/day at the second examination.

Table 3 displays age-adjusted incidence rates and numbers of deaths for men and women separately according to smoking group and the type of tobacco smoked. All-cause mortality and mortality from cardiovascular disease, smoking-related cancers, and respiratory disease (chronic obstructive pulmonary disease and pneumonia) are shown.

Results from the Cox regression analyses are presented in table 4. Adjusted hazard ratios and 95 percent confidence intervals for all-cause mortality are shown for cigarette

TABLE 2. Characteristics of participants at their second examination according to smoking status for the pooled study population (*n* = 19,732), Copenhagen Centre for Prospective Population Studies, Denmark, 1976–2000

Characteristic	Never smokers (*n* = 4,002)	Ex-smokers (*n* = 2,850)	Quitters (*n* = 1,467)	Light smokers (*n* = 3,319)	Reducers (*n* = 858)	Heavy smokers (*n* = 7,236)	*p* value*
Sex (% men)	33.7	65.8	61.1	47.5	72.6	66.9	0.001
Mean age (years)	54.5 (12.3)†	55.8 (11.0)	55.1 (11.6)	55.0 (10.9)	55.2 (11.1)	52.3 (9.9)	<0.001‡
Mean tobacco consumption (g/day)				9.6 (4.5)	8.5 (5.2)	20.3 (8.9)	<0.001‡
Mean duration of smoking (years)			29.2 (14.3)	31.9 (13.1)	35.8 (12.0)	34.0 (10.7)	<0.001‡
Inhalers (%)				60.0	62.9	72.2	<0.001
Tobacco type (%)							
Cigarettes				61.2	52.4	58.2	<0.001
Cigars, cheroots, pipes, or mixed types				38.8	47.6	41.8	<0.001

* *p* value for the difference between those who reduced their smoking and those who continued to smoke heavily.
† Numbers in parentheses, standard deviation.
‡ Two-sample *t* tests. All other tests were Pearson chi-squared tests.

smokers only and for smokers of other tobacco products, whereas estimates of cause-specific mortality are presented for cigarette smokers alone. There were significantly reduced mortality risks in cigarette smokers who stopped smoking between the first two examinations and in light smokers, regardless of the type of tobacco smoked. In contrast, cigarette smokers who reduced their smoking experienced an all-cause mortality risk similar to that of sustained heavy smokers (hazard ratio (HR) = 1.02, 95 percent confidence interval (CI): 0.89, 1.17). A small but nonsignificant risk reduction was suggested for smokers of cigars, cheroots, or pipes who reduced their smoking (HR = 0.87, 95 percent CI: 0.70, 1.08).

Hazards for cardiovascular mortality revealed a pattern similar to that for all-cause mortality: Participants who reduced their smoking had a risk close to unity in comparison with persistent heavy smokers, whereas light smoking and quitting smoking showed a trend towards reduced risk. For tobacco-related cancers, there was stronger evidence of a dose-response relation: Persons who quit smoking or were

TABLE 3. Age-adjusted mortality rates (per 1,000 person-years) and numbers of deaths, by smoking status, tobacco type, and sex, for deaths from all causes, cardiovascular disease, tobacco-related cancers, and respiratory disease in the pooled study population (*n* = 19,732), Copenhagen Centre for Prospective Population Studies, Denmark, 1978–2000

Cause of death	Never smokers	Ex-smokers	Quitters		Light smokers		Reducers		Heavy smokers	
			Cigarettes	Other type of tobacco	Cigarettes	Other type of tobacco	Cigarettes	Other type of tobacco	Cigarettes	Other type of tobacco
Total no. of deaths	1,049	948	577		1,073		434		3,136	
Person-years of follow-up	56,566	39,425	19,556		44,648		11,479		97,634	
All-cause mortality										
Men	22.0 (336)*	25.1 (704)	30.2 (240)	40.8 (149)	33.9 (401)	32.1 (152)	42.4 (246)	41.8 (84)	39.4(1831)	42.0 (504)
Women	15.0 (713)	14.7 (244)	20.1 (120)	21.1 (68)	21.4 (466)	22.6 (54)	32.8 (66)	32.6 (38)	28.3 (616)	31.7 (185)
Cardiovascular disease										
Men	7.4 (112)	8.5 (252)	11.4 (89)	11.2 (40)	10.5 (112)	10.0 (26)	13.5 (71)	13.4 (53)	11.3 (538)	11.3 (268)
Women	4.9 (255)	3.8 (76)	5.8 (39)	2.4 (3)	5.4 (112)	2.5 (1)	6.3 (14)	0	6.3 (136)	11.1 (11)
Tobacco-related cancers										
Men	1.6 (25)	1.7 (51)	3.6 (29)	4.3 (15)	4.7 (50)	6.0 (17)	7.1 (36)	6.4 (23)	7.7 (372)	6.4 (151)
Women	0.8 (33)	0.8 (15)	1.2 (7)	0	2.4 (46)	0	5.2 (10)	4.0 (1)	4.8 (120)	3.1 (6)
Respiratory disease										
Men	0.7 (10)	1.0 (29)	1.3 (10)	0	2.5 (26)	0	2.4 (13)	2.2 (9)	2.2 (96)	1.8 (38)
Women	0.4 (21)	0.3 (7)	1.7 (10)	0.7 (3)	1.4 (29)	1.6 (4)	3.6 (6)	0	2.3 (51)	0.4 (2)

* Numbers in parentheses, number of deaths.

TABLE 4. Hazard ratios* for all-cause and cause-specific mortality during follow-up for different smoking groups as compared with persons who continued to smoke heavily (hazard ratio = 1), Copenhagen Centre for Prospective Population Studies, Denmark, 1978–2000

Cause of death	Cigarette smokers only			Cigar, cheroot, and pipe smokers†	
	No. of deaths	Adjusted HR‡	95% CI‡	Adjusted HR	95% CI
All causes					
Reducers	434	1.02	0.89, 1.17	0.87	0.70, 1.08
Quitters	577	0.65	0.56, 0.74	0.91	0.75, 1.11
Light smokers	1,073	0.75	0.69, 0.82	0.65	0.54, 0.77
Cardiovascular disease§					
Reducers	138	1.01	0.76, 1.35		
Quitters	171	0.88	0.68, 1.15		
Light smokers	251	0.91	0.76, 1.08		
Tobacco-related cancer					
Reducers	70	0.91	0.63, 1.31		
Quitters	51	0.36	0.22, 0.59		
Light smokers	113	0.53	0.41, 0.69		
Respiratory disease					
Reducers	28	1.20	0.70, 2.07		
Quitters	23	0.77	0.44, 1.35		
Light smokers	59	0.77	0.54, 1.09		

* Results were obtained from a stratified Cox proportional hazards regression model, with data adjusted for age (underlying), sex, cohort of origin, body mass index (weight (kg)/height (m)^2) in four categories (<20, 20–24, 25–29, ≥30), educational level in three categories (<8 years, 8–11 years, ≥12 years), duration of smoking (in 1-year units), and inhalation habits (yes/no).

† Because of few deaths among smokers of types of tobacco other than cigarettes, analyses in this group were restricted to all-cause mortality.

‡ HR, hazard ratio; CI, confidence interval.

§ The analyses included adjustment for systolic blood pressure (per 10-mmHg increase).

light smokers had 64 percent (HR = 0.36, 95 percent CI: 0.22, 0.59) and 47 percent (HR = 0.53, 95 percent CI: 0.41, 0.69) reductions in mortality risk, respectively. Those who reduced their smoking did not have a significantly lower risk of death from tobacco-related cancers in comparison with continuous heavy smokers.

The analyses of mortality from chronic obstructive pulmonary disease and pneumonia were based on very few deaths among reducers and quitters. There was an insignificant increase in mortality risk of 20 percent for the reducers (HR = 1.20, 95 percent CI: 0.70, 2.07) in the fully adjusted model. Quitting smoking or smoking lightly was associated with reductions in risk of mortality from respiratory diseases of approximately 25 percent, but none of the computed estimates reached statistical significance.

DISCUSSION

To our knowledge, this large prospective cohort study with almost 16 years of follow-up was the first to examine the associations of mortality from all causes and mortality from tobacco-related diseases with unassisted smoking reduction. We found no significant differences in mortality from all causes, cardiovascular diseases, tobacco-related cancers, or respiratory diseases between subjects who reduced their smoking considerably and subjects who continued to smoke heavily, although there was a slight trend towards reduced risk for cancer mortality and for smoking types of tobacco other than cigarettes. However, the effects of smoking reduction on tobacco-related cancers were far smaller than those resulting from sustained light smoking or smoking cessation. Thus, we cannot confirm the hypothesis that a decrease in the daily amount of tobacco smoked from a level comparable to that of continuous heavy smokers to a level comparable to that of continuous light smokers corresponds to a decrease in mortality similar to (or close to) the risk of light smokers. On the other hand, estimates of mortality risk in the other ever-smoking groups (quitters and light smokers) were consistent with the literature, which supports our findings in general.

It is possible that the reducers had already accumulated harmful substances in their bodies from their previously more intense smoking habit, precluding this "reversed dose-response." Furthermore, it might be hypothesized that the reversibility of the damage, which might explain the benefits derived from smoking cessation (29), does not apply to smokers who reduce their intake. Hence, in this group of diseases with a complex and multifactorial etiology, the

impact of smoking reduction may not be substantial enough to show a proportional reduction in mortality.

Previous studies from this population have shown substantial gender differences in morbidity and mortality from cardiovascular diseases (30, 31). However, in comparing cardiovascular mortality in the various groups of smokers, we stratified the analyses, allowing baseline hazards to differ between men and women.

There is a huge amount of evidence from prospective studies regarding the benefits of smoking cessation, in terms of decreased risk of mortality from coronary heart disease and vascular diseases (1), whereas the magnitude of the gain and the time required to prove results is still debatable. In the Whitehall Study, former smokers had a persistently elevated risk of coronary heart disease up to 30 years after quitting smoking (32), whereas in a large Norwegian study (33), coronary heart disease mortality decreased among men who had stopped smoking to nearly the level of never smokers after 5 years or more. Findings from the Nurses' Health Study and two recent papers also suggested that after 10 or more years of smoking cessation, mortality risk is attenuated to the level of never smokers (34–36).

With respect to tobacco-related cancers, our results indicated a clear benefit from quitting smoking. With the somewhat unexpected exception of results from 10 and 16 years of follow-up in the Multiple Risk Factor Intervention Trial (37, 38), smoking cessation is well known to reduce cancer risk, although there is a considerable time lag before decreases in cancer incidence are seen in comparison with cardiovascular events. Recently, it was estimated by Peto et al. (39) that quitting smoking before middle age is associated with a greater than 90 percent reduction in tobacco-attributable cancer risk. For smoking reduction, there are no existing epidemiologic data, while one study has shown that levels of one out of three carcinogenic biomarkers decreased significantly after 24 weeks of reduced smoking (25).

Our analysis of smoking reduction and mortality from chronic obstructive pulmonary disease and pneumonia was based on the smallest number of deaths, and no estimates in any of the smoking groups were significant for this endpoint, possibly because of lack of power. However, our results indicated a small increase in risk for persons who reduced their smoking as compared with sustained heavy smokers, while quitters had a decreased risk. Respiratory disease morbidity and mortality is also known to decrease after smoking cessation, mediated through a reduced decline in forced expiratory volume in 1 second, even among subjects with established chronic obstructive pulmonary disease (40), and the well-established beneficial effect of smoking cessation (41–43) is also apparent for quitters in the present study. It is likely that the processes initiated by heavy smoking are not substantially altered in the smoking reducer, who is still susceptible to the harmful effects of smoking on the lungs and airways. This is supported to some extent by findings showing that the beneficial effect of smoking cessation on lung function decline is smaller once significant airflow limitation has been established (44, 45).

This study had several advantages. It was large, it included a large proportion of heavy smokers at baseline, and it had almost 100 percent complete follow-up. As in any cohort study that examines changes in risk factor exposure, the question of residual and unmeasured confounding becomes relevant. We focused on the comparison between reducers and sustained heavy smokers, but our study design did not enable us to examine reasons for this change in smoking behavior. Thus, we do not know whether the reducing group actually comprised subjects who were unable or unwilling to quit altogether. We have previously shown that heavy smokers who reduce their smoking differ in some ways from continuously heavy smokers (16), which suggests that the reducers generally have a less healthy lifestyle. However, we tried to account for this through exclusion of the initial deaths and through detailed stratification and adjustment for differences in smoking experience.

Another issue is compensatory smoking. Generally, reduction in intake is not followed by a corresponding decrease in intake of harmful substances from cigarette smoke, probably because the smoker smokes the remaining cigarettes more intensely (13). In a recent clinical trial of smoking reduction using nicotine replacement therapy, a decrease in self-reported number of cigarettes per day of 38–45 percent was achieved, but carbon monoxide levels were only decreased by 19–20 percent and measures of cotinine and thiocyanate were unchanged (46). Other longitudinal studies have pointed out that some underestimation of benefits from smoking cessation could occur because of relapse among quitters, usually within the first few years after cessation (32). Regarding reducers, the data we had on smoking behavior from the examination following reduction (an elapsed time of about 10 years) indicated that approximately 50 percent of these subjects continued to smoke as light smokers, 20 percent quit smoking entirely, and the remaining 30 percent relapsed to heavy smoking. This also confirms that maintenance of smoking reduction is possible and that resumption of heavy smoking in our study cannot explain the absence of results. Nevertheless, in this study, we had to rely on the subjects' accuracy in reporting their tobacco habits, and our results could have been biased because of differential misclassification, especially if the reducers tended to under- or misreport their consumption.

In summary, we have shown that the long-term effects of a substantial reduction in smoking did not show any benefits in comparison with persistent heavy smoking with respect to all-cause and cause-specific mortality. Mortality risk showed a dose-response relation with amount smoked, and smoking cessation was associated with a reduced mortality risk. Clearly, since this was the first prospective population study to address this question, more research is needed. Results from studies of large cohorts would be useful in either confirming or rejecting our findings.

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