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ORIGINAL ARTICLE

Smoking Cessation and Short- and Longer-Term Mortality

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Abstract

BACKGROUND Smoking cessation reduces mortality and morbidity. However, the extent and rapidity at which cessation reduces contemporary death rates from smoking-related illnesses remain uncertain.

METHODS We pooled current or former versus never cigarette smoker hazard ratios from four national cohorts with linkage to death registries in the United States, United Kingdom, Norway, and Canada among adults 20 to 79 years of age from 1974 to 2018. We calculated excess risk differences and survival, comparing current or never smokers with age-specific cessation and cessation fewer than 3, 3 to 9, or 10 or more years earlier.

RESULTS Among 1.48 million adults followed for 15 years, 122,697 deaths occurred. Adjusting for age, education, alcohol use, and obesity, current smokers had higher hazard ratios for death compared with never smokers (2.8 for women, 2.7 for men). Survival between 40 and 79 years of age was 12 and 13 years less in women and men, respectively, who smoked compared with never smokers (about 24 to 26 years of life lost for smokers who died from smoking combined with zero loss for smokers who did not die from smoking). Former smokers showed lower hazard ratios (1.3 in both women and men). Short-term cessation for fewer than 3 years was associated with a lower excess risk of 95% in women and 90% in men younger than 40 years of age, with notable beneficial associations also in women and men 40 to 49 years of age (81% and 61%, respectively) and 50 to 59 years of age (63% and 54%, respectively). Cessation at every age was associated with longer survival, particularly cessation before 40 years of age. Among all ages and compared with continued smoking, cessation of fewer than 3 years potentially averted 5 years of life lost and cessation for 10 or more years averted about 10 years of life lost, yielding survival similar to that of never smokers.

CONCLUSIONS Quitting smoking at any age, but particularly in younger years, was associated with lower excess mortality overall and from vascular, respiratory, and neoplastic diseases. Beneficial associations were evident as early as 3 years after cessation. (Funded by Canadian Institutes of Health Research [FDN-154277].)

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Introduction

Prolonged cigarette smoking remains a major cause of premature death worldwide, accounting for 5 to 7 million deaths annually.[1-3] Despite substantial declines in adult smoking prevalence, smoking still causes at least a quarter of all deaths in middle-aged adults in Europe and North America.[4] The considerable number of adults who have quit smoking in recent decades[3-7] affords an opportunity to document the extent to which cessation reduces contemporary mortality rates from the various smoking-attributable diseases.

Cessation by 40 years of age averts 90% of the lifetime risk of mortality attributable to smoking compared with continued smoking.[2-5] Smokers considering quitting would benefit from understanding not only the lifetime reduction in risk, but also the extent and rapidity at which cessation reduces their short-term mortality risk, as well as understanding the short- and longer-term reductions in the major diseases caused by smoking.[7,8]

Here, we quantify the potential benefits of smoking cessation by age, sex, and years since stopping on cause-specific mortality using four large national observational cohorts. The high-income countries we examine have diverse tobacco mortality patterns and cessation rates.

Methods

STUDY DESIGN

We conducted an individual-level meta-analysis of four large national observational health cohorts with linkage to death registries. Each cohort has extensive documentation of their detailed sampling strategy, survey procedures, and refusal rates, as well as linkage to national mortality data. The first two are nationally representative. The National Health Interview Survey (NHIS) captures a representative sample of the U.S. civilian, noninstitutionalized population 20 to 79 years of age, enrolling a rolling sample of households annually; we used data from the 1997–2018 survey samples.[3,9] Similarly, the Canadian Community Health Survey (CCHS) recruited adults 20 to 79 years of age annually from a rolling sample of households; we used data from the 2000–2014 samples.[10] In Norway, we merged three cohort studies initiated between 1974 and 2003 that recruited participants 25 to 79 years of age to constitute the Norwegian Health Screening Survey Cohorts.[11,12] These include the Counties Study (1974 to 1988), 40 Years Study (1985 to 1999), and Cohort of Norway (1994 to 2003).[13,14] The U.K. Biobank recruited adults 40 to 73 years of age from 2006 to 2010. U.K. Biobank participants, invited within the U.K.'s universal health system, are not nationally representative but do capture diverse geographic settings and social groups.[15,16]

POPULATIONS OBSERVED

We defined current smokers as those who smoked cigarettes daily or on some days at the time of the enrollment survey and former smokers as those who had smoked at least 100 cigarettes in their lifetime, capturing how many years before enrollment they had quit. Never smokers consumed fewer than 100 cigarettes in their lifetime. Other recorded variables included education level, height and weight (self-reported, except in Norway, where nurses measured these at screening), and alcohol consumption (except in Norway, where questions on drinking were included only from 1994 onward among only 27% of the three cohorts and are excluded from the current analyses).[11]

OUTCOMES

Each of the cohorts conducts linkage between their enrolled populations and national death registries, which provide cause-specific mortality. About 85% and 95% of the CCHS and NHIS enrollees, respectively, consented to linkage to national death registries, with linkage based on name, date of birth, age, sex, and social insurance/security numbers.[10,17,18] The U.K. Biobank sends a list of all participants using national health identification numbers and other personal details for linkage quarterly to national digital registers in England, Wales, and Scotland.[19] Norway's national 11-digit unique personal identification number enables linkage of these cohorts to national cause-of-death registries.[11,12]

All four national death registers provide detailed information on the underlying and multiple causes of death, using the International Classification of Diseases, 10th edition (ICD-10).[20] Evaluations of each cohort and their linkage with their respective death registries have determined high follow-up rates, matching more than 95% of individual death records with cause-specific mortality, except for the small number who migrated to other countries.[9-19] The major categories of smoking-attributable diseases[2,3,21] were vascular, respiratory, and neoplastic (cancer) mortality and all-cause mortality (which includes nonmedical causes such as accidents and suicide; see Table S1 in the Supplementary Appendix for ICD-10 codes). Current or former smoker versus never smoker associations for all-cause mortality should be unaffected by potential misclassification of causes.

CALCULATION OF EXCESS AND ABSOLUTE RISK REDUCTIONS

For each national cohort, we fit Cox proportional hazard models[22] for current and former smokers (examining separately cessation of <1, <3, 3 to 9, or ≥10 years' duration) for each outcome of interest. We calculated hazard ratios for current smoker:never smoker (HRc) and former smoker:never smoker (HRf), adjusting for education (less than high school, high school, more than high school), alcohol drinking (never, former, or light drinker [one to two drinks a day for women or one to three drinks a day for men], or heavy drinker [three or more drinks a day for women or four or more drinks a day for men]), and body mass index (BMI [the weight in kilograms divided by the square of the height in meters]; <25, 25 to <30, and ≥30). Because the cohorts did not capture information about cessation after enrollment, observed hazard ratios using baseline smoking status would tend to underestimate the true hazards of continued smoking.[5] To calculate quitting-adjusted HRc, we examined the age- and sex-specific proportion of smokers who had quit by 3 years before enrollment in each cohort and applied this to estimate quitting after enrollment. Quitters should have the hazards of former smokers (HRf). By contrast, smokers who did not quit should have the true (quitting-adjusted) hazards of continued smoking (HRc). This yields $HRc = (HRuncorrected - p*HRf)/(1 - p)$, where p is the proportion of quitters. Table S2 and Figure S1 show recent quitters by age and sex ranging from 10 to 16% in the pooled results, and Table S3 provides the corrected and uncorrected hazard ratios for overall mortality from current smoking for each cohort.

We pooled hazard ratios across the four national cohorts for each age group (<40, 40 to 49, 50 to 59, 60 to 69, and 70 to 79 years of age) and sex for current and former smokers using random effects meta-analyses[23] with similar results if cohorts were weighted by their number of events (data not shown). Using the pooled results, we calculated the excess risk difference from cessation of various durations as $1 - [(HRf - 1)/(HRc - 1)]$. We calculated the absolute risk differences as the difference between risks of death among current smokers versus former smokers, focusing on risks of death between 40 and 79 years of age. We derived each risk from death rates, which for current smokers was calculated by multiplying the death rates in never smokers by the adjusted HRc (to account for potential confounders and some effects of cessation after enrollment). The Supplementary Appendix provides the statistical methods, including details of the meta-analyses. We used SAS version 9.4 (SAS Institute, Cary, NC) and R version 3.6.0 for the analyses.

Results

The four national cohorts included 1.48 million adults with a mean follow-up time of 14.8 years and recorded 122,697 deaths during 23.0 million person-years of follow-up (Table 1; additional details in Tables S1 and S4). In each cohort, compared with never smokers, current smokers had less education, more alcohol use, and lower BMI (Table S1). Compared with never smokers, former smokers had less education, more alcohol use, and higher BMI, except Norwegian women, in whom BMI was similar. Hence, subsequent analyses adjusted for these differences. The current versus never smoker hazard ratios for overall mortality were 2.8 (99% confidence interval [CI], 2.2 to 3.6) for women and 2.7 (2.2 to 3.4) for men, ranging from 2.2 to 3.7 in women and 2.3 to 3.9 in men across the studies (Table 1). Among current smokers, heavy smoking (≥20 cigarettes/day) was more common in men (32.4%) than in women (19.8%), but women had slightly higher hazard ratios for overall mortality for heavy smoking (Table S3).

EXCESS RISK REDUCTIONS FOLLOWING SMOKING CESSATION

The hazard ratios (99% CIs) for overall mortality for any former versus never smoker (1.3 [1.1 to 1.5] for each sex) were half the corresponding hazard ratios for current smokers (Table 1, Fig. 1, and Table S5). Hazard ratios for overall mortality among heavy former smokers were slightly higher than among any former smokers, especially among women (Table S3). At all ages, we observed the highest hazard ratios for current smokers for deaths from respiratory disease (women, 7.6; men, 6.3), followed by vascular disease (women, 3.1; men, 2.9) and cancer (women, 2.8; men, 3.1). Respiratory disease showed the highest hazard ratios for former smokers and vascular disease the lowest (1.9 and 1.2, respectively, in each sex). For overall mortality and in each sex, the excess hazard (defined as hazard

Table 1. Characteristics of National Cohorts and Baseline Characteristics of Participants.*

Characteristic	U.K. Biobank	Norway NHSSC	U.S. NHIS	Canada CCHS	All Studies
Survey years	2006–2010	1974–2003	1997–2018	2000–2014	1974–2018
Follow-up years/person-years — mean (millions)	12.5/5.0	20.3/11.8	11.9/4.6	14.4/1.7	14.8/23.0
Age range — yr	40–73	25–79	20–79	20–79	20–79
No. of men/women observed	179,254/217,140	278,776/300,034	179,780/207,314	54,721/60,562	692,531/785,050
No. of men/women who died	15,297/10,609	38,336/27,781	11,870/10,727	4,446/3,631	69,949/52,748
Smoking — % of men/women					
Current smoker	13.7/9.8	40.1/38.2	24.1/17.9	31.7/24.4	28.4/23.9
Former smoker	31.4/23.8	26.3/21.0	22.2/16.3	35.3/28.8	27.3/21.1
Smoking, men/women vs. never smokers — hazard ratio (99% CI)					
Current smoker — men/women	2.9 (2.8–3.1)/ 3.2 (3.0–3.4)	2.3 (2.2–2.4)/ 2.2 (2.1–2.3)	2.3 (2.1–2.4)/ 2.5 (2.3–2.6)	3.9 (3.4–4.4)/ 3.7 (3.3–4.1)	2.7 (2.2–3.4)/ 2.8 (2.2–3.6)
Former smoker — men/women	1.4 (1.3–1.4)/ 1.4 (1.3–1.4)	1.1 (1.1–1.2)/ 1.1 (1.1–1.2)	1.2 (1.1–1.3)/ 1.2 (1.1–1.3)	1.5 (1.3–1.7)/ 1.5 (1.3–1.7)	1.3 (1.1–1.5)/ 1.3 (1.1–1.5)

* The hazard ratio was adjusted for age, education, body mass index, and alcohol consumption (except in Norway). The smoking amount was not reported in the U.S. NHIS. CCHS denotes Canadian Community Health Survey; CI, confidence interval; NHSSC, Norwegian Health Screening Survey Cohorts; and NHIS, National Health Interview Survey.

ratio-1) among any former smokers (0.3) was more than 80% lower than the excess hazards among current female and male smokers (1.8 and 1.7, respectively; Fig. 1).

The appropriate measurement of difference in excess risk between former and current smokers must consider age at quitting and not only age at enrollment, as well as time since quitting. We examined the excess risk differences by age group considering the duration of cessation and adjusting for covariates; our data showed that adjustment for these characteristics made little difference in excess risk estimates. Considering overall mortality at 50 to 59 years of age, by which peak cessation occurred in each country (Fig. S1), excess risk differences were larger in women and men for cessation of fewer than 3 years ago, at 63% and 54%, respectively, than they were for cessation of less than 1 year ago, at 51% and 43%, respectively (Table 2 and Table S6). We saw a similar pattern of larger excess risk difference with cessation of fewer than 3 years versus less than 1 year in each sex and most age groups, except for men younger than 50 years of age.

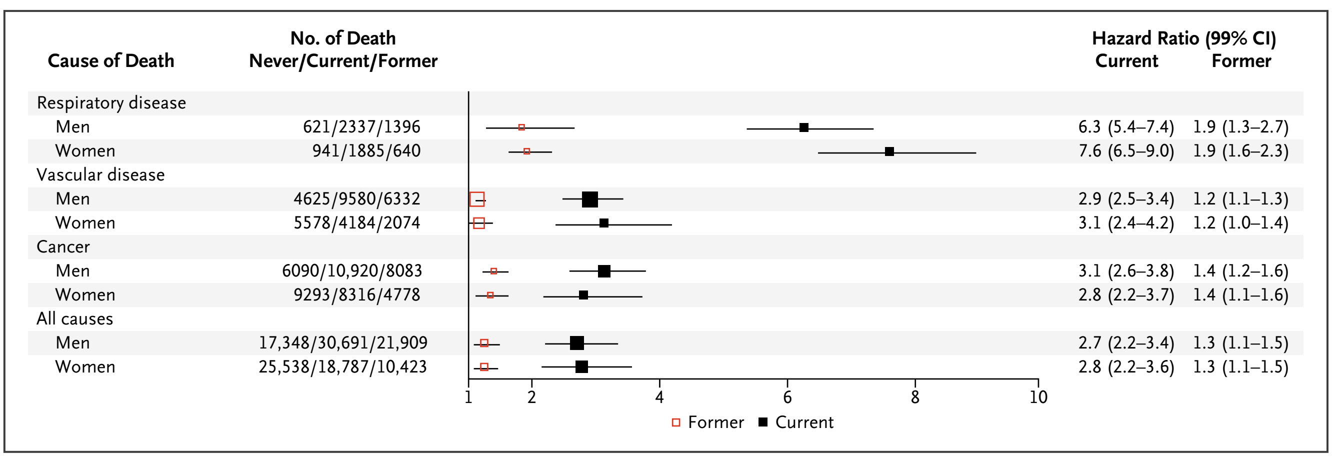

Figure 1. Hazard Ratios Comparing Current and Former Smokers with Never Smokers by Cause of Death and Sex in Pooled Analyses of Four National Cohorts.

The area of each square is inversely proportional to the variance of the log of the hazard ratio. CI denotes confidence interval.

Table 2. All-Cause Mortality ERD among Former Smokers of Fewer Than 3-Year Cessation Duration Compared with Current Smokers, by Sex and Age Group.*

	Men				Women			
Age (yr)	No. of Never/Current/ Former Smokers	Current Smokers — Hazard Ratio (99% CI)	Former Smokers — Hazard Ratio (99% CI)	ERD — % (99% CI)	No. of Never/Current/ Former Smokers	Current Smokers — Hazard Ratio (99% CI)	Former Smokers — Hazard Ratio (99% CI)	ERD — % (99% CI)
<50	7,086/19,266/1,215	2.39 (1.99–2.86)	1.41 (1.11–1.78)	71 (46–96)	7,458/11,370/568	2.26 (1.97–2.60)	1.21 (1.04–1.41)	83 (68–98)
50–59	2,392/3,468/336	3.12 (2.77–3.53)	1.98 (1.61–2.43)	54 (33–75)	2,527/2,023/176	2.92 (2.46–3.46)	1.71 (1.31–2.23)	63 (38–89)
60–79	7,870/7,957/997	2.35 (1.94–2.84)	1.90 (1.52–2.37)	33 (0–71)	13,553/5,394/651	2.52 (1.95–3.27)	1.91 (1.44–2.54)	40 (0–84)

* The results comparing cessation less than 1 year, adjustment for education only, and excluding the first 3 years of follow-up are shown in Table S3. The 99% CIs for the ERD are wide because they consider both the current-to- never-smoker and the former-to-never-smoker hazard ratios (see Methods in the Supplementary Appendix). CI denotes confidence interval; ERD, excess risk differences, adjusted for education, body mass index, and alcohol (except for Norwegian study).

Reverse causality, which is some aspect of ill health that causes some smokers to quit reasonably close to enrollment, is more likely in very recent quitters of less than a year. In addition, a small proportion of very recent quitters may have relapsed to smoking. Thus, we believe that cessation fewer than 3 years earlier is a more robust measure of the short-term benefits of cessation. Cessation fewer than 3 years yielded excess risk differences similar to those observed if we excluded the first 3 years of follow-up to reduce possible reverse causality (Table S6). Excess risk differences with or without additional adjustment for alcohol use or BMI, performed to consider residual confounding, yielded very similar hazard ratios to those adjusted for age and education (Table S4).

The excess risk differences for overall mortality for cessation fewer than 3 years were highest for younger adults and progressively smaller at older ages. Women and men who quit before 40 years of age or younger had death rates close to never smokers, potentially averting 95% and 90%, respectively, of the continued risk of smoking. The female/male excess risk differences were 63%/54% at 50 to 59 years of age and 40%/33% at 60 to 79 years of age. The latter two decades were combined because there was little cessation beyond 70 years of age. The excess risk differences for cessation 3 to 9 years were 72%/64% for women/men at 50 to 59 years of age, respectively. The excess risk differences for cessation 10 years or more were 95%/92% for women/men at 50 to 59 years of age, respectively (Fig. 2). For both sexes, the rank order, largest to smallest, for differences by cause of death was vascular disease, followed by cancer, with the lowest for respiratory disease. Differences were generally larger among women than men but with overlapping CIs because there was uncertainty in the hazard ratios in both current and former smokers. By contrast, the absolute risk differences for cessation of any duration were the largest at older ages, reflecting the higher background death rates at these ages. For overall mortality, the absolute risk differences in women/men for cessation less than 3 years at 60 to 79 years of age were 8.2%/6.5%, compared with 1.3%/1.8% for less than 40 years of age (Fig. S2).

CUMULATIVE SURVIVAL FOLLOWING CESSATION

The pooled analyses showed cumulative survival from 40 to 79 years of age between never smokers and current smokers of 83% versus 59% in men with an absolute gap of 24 percentage points and 87% versus 67% in women with an absolute gap of 20 percentage points (Fig. S3). These mortality risks equate to an average of 12 and 13 years of potential life lost in female and male smokers, respectively, compared with otherwise similar never smokers. This loss combines approximately 24 to 26 years of life lost for smokers who died as a result of smoking with a zero loss for smokers who did not die from smoking. The average potential loss of life attributable to smoking for current versus never male/female smokers was 14/10 years for vascular diseases, 12/12 years for cancer, and 18/20 years for respiratory disease (Table 3).

Among smokers of all ages, cessation of 10 or more years yielded survival comparable to that of never smokers, averting about 10 years of life lost from all causes. Cessation of 10 or more years yielded survival improvements of 8 to 15 years, depending on the major disease categories and on sex (Table 3). Much of the eventual longer-term survival improvements accrued within a short time frame. Cessation fewer than 3 years potentially averted about 5 years of life lost from continued smoking, with variation by causes (Table 3 and Fig. S3).

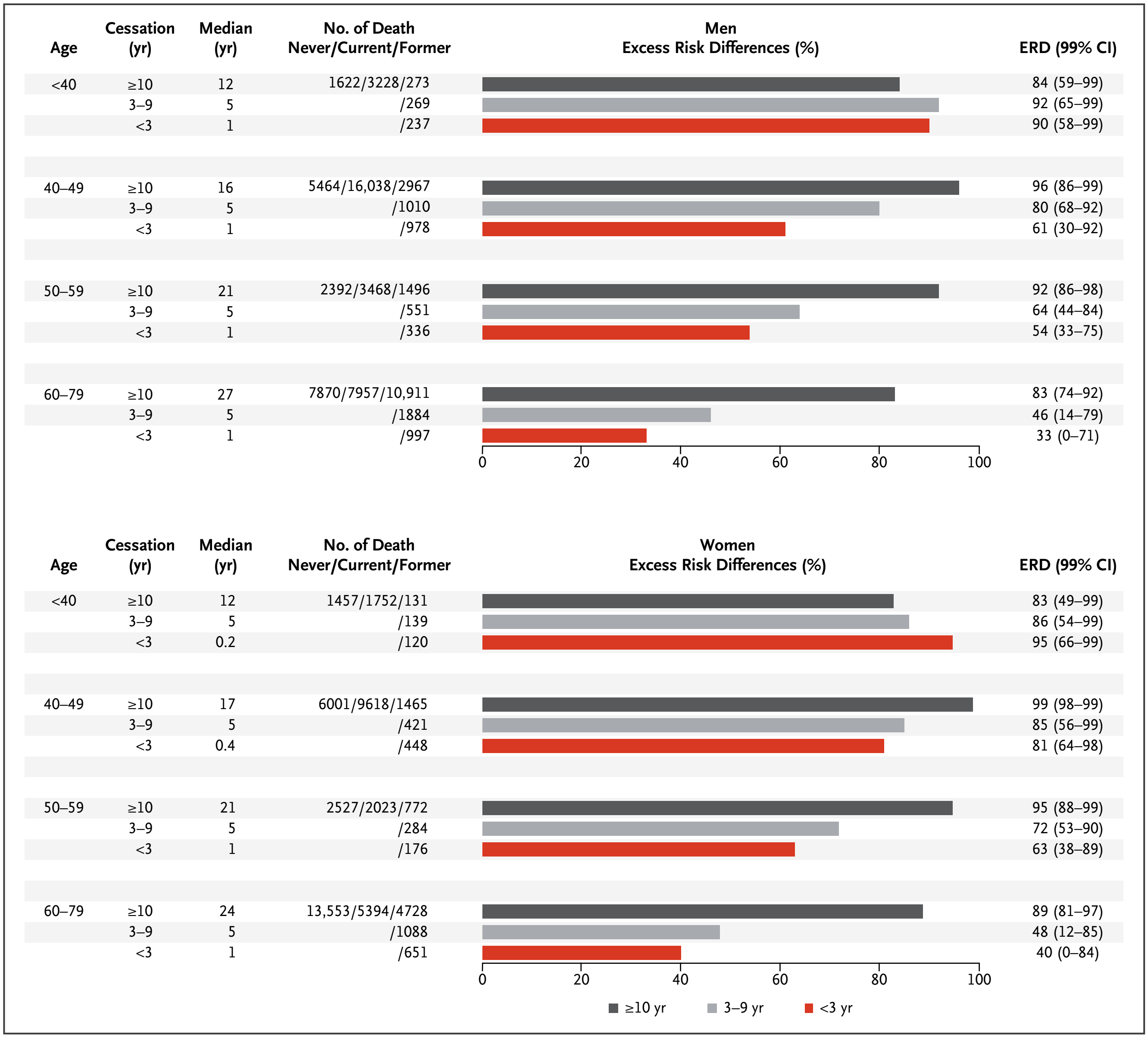

Figure 2. Excess Risk Differences for Cessation 10 Years or More, 3 to 9 Years, and Fewer Than 3 Years Earlier Compared with Never Smokers for Overall Mortality by Age Group and Sex in Pooled Analyses of Four National Cohorts.

CI denotes confidence interval; ERD, excess risk difference; No., number; and yr, year.

In the pooled analyses, the survival to 80 years of age was greatest for quitting before 40 years of age (12-year gain), followed by quitting at 40 to 49 years of age (6-year gain), but still notable even for cessation at 50 to 59 years of age (2.5-year gain; Fig. 3). Differences in survival from cessation were similar in women and men.

Discussion

Our analyses pooling four large national cohorts with linkage to death registries in high-income countries provide contemporary evidence that cessation of smoking at any

Table 3. Years of Life Expectancy Gained between 40 and 79 Years of Age in Relation to Duration of Quitting Smoking by Sex and Cause of Death.*

	Former Smokers vs. Current Smokers by Duration of Quitting, yr				Never Smokers vs. Current Smokers, yr	
	Men		Women		Men	Women
Cause of Death	<3	≥10	<3	≥10		
All causes	5.5	9.9	5.1	9.6	12.9	11.8
Vascular disease	7.0	12.1	5.2	9.4	14.3	10.1
Cancer	4.5	8.2	4.6	8.7	12.3	12.0
Respiratory disease	7.5	12.3	9.9	15.1	17.5	20.2

* The data were derived from life table estimates based on death rates adjusted for age, education, body mass index, and alcohol consumption (except in Norway).

age, but particularly before 40 years of age, is associated with lower excess risk of mortality, both overall and from the major diseases made more common by smoking. Sustained cessation in former smokers is associated with death risks approaching those of never smokers over a lifetime. Importantly, much of large long-term associations of cessation and mortality occur early, within a few years of cessation.

Many individual smokers erroneously believe that cessation will not help them because they have been lifelong or heavy smokers.[7,8] We document lower excess risk in vascular and cancer mortality but less so for respiratory mortality, likely reflecting long-term irreversible airway damage.[2,3,21,24] Moreover, although the smoker:never smoker hazard ratios varied only slightly by age, the absolute risk differences associated with cessation increased with age.

Our quantification of the hazards of smoking and potential benefits of cessation can inform individuals, health care providers seeking to raise cessation rates within their patient populations, and population-based strategies.[2,25] Even with substantial increases in smoking cessation in the United States, Canada, United Kingdom, and Norway, there were still 60 million smokers over 15 years of age in those countries as of 2019.[6] Moreover, quit rates are substantially lower in low socioeconomic groups.[21,26] Given higher rates of smoking-attributable and background death rates in the lowest social strata, increases in cessation across all income groups are likely to reduce the absolute social inequalities in mortality.[27] We focused on high-income countries, but our results also inform the more than 1 billion smokers worldwide on the benefits of cessation, given that smokers in both high-income and low- and middle-income countries who start early in adult life and do not quit face similar hazards.[1-3,25]

Because continuing smoking is so exceptionally hazardous, quitting yields large benefits, particularly as the medium-term death rates among nonsmokers have fallen in the last two decades in many countries.[28] Cost-effective interventions to encourage cessation include higher excise taxes on tobacco products, particularly on shorter, cheaper cigarettes that the tobacco industry promotes to recruit adolescents and reduce cessation; nicotine-based strategies and quit-smoking medicines; and bans on tobacco advertising, promotion, and smoking in public places.[1,25,29,30]

Our study has some limitations. First, ever smokers and never smokers differ beyond the few variables we measured. However, adjustment for education, alcohol, and BMI did little to alter the hazard ratios, signifying that most of the association between smoking and cause-specific mortality is probably — but not definitively — causal.[3,21] Second, some excess mortality among former smokers might be overestimated because it reflects deaths in smokers who quit because they became ill. However, excluding deaths during the first few years of follow-up yielded similar results to our main analyses. Although we adjusted the hazards of current smoking to consider quitting 3 years or less after enrollment, enrolled smokers continue to quit. In the U.K. Million Women study, about 40% of baseline smokers quit by year 8, with annual declines in the first 3 years of follow-up being nearly twice as fast as in the subsequent 5 years.[5] The re-surveys of the U.K. Biobank also showed substantial cessation after enrollment, with the fastest decline soon after enrollment.[31] Smoking prevalence declined in all four study countries during the study periods.[6] If the true hazards of current smoking are even greater than we observed, the relative and absolute risk differences arising from cessation will be more favorable than we estimated. Indeed, our procedure to consider cessation after enrollment avoids the likely underestimation of current:never smoker hazard differences.[32] Third,

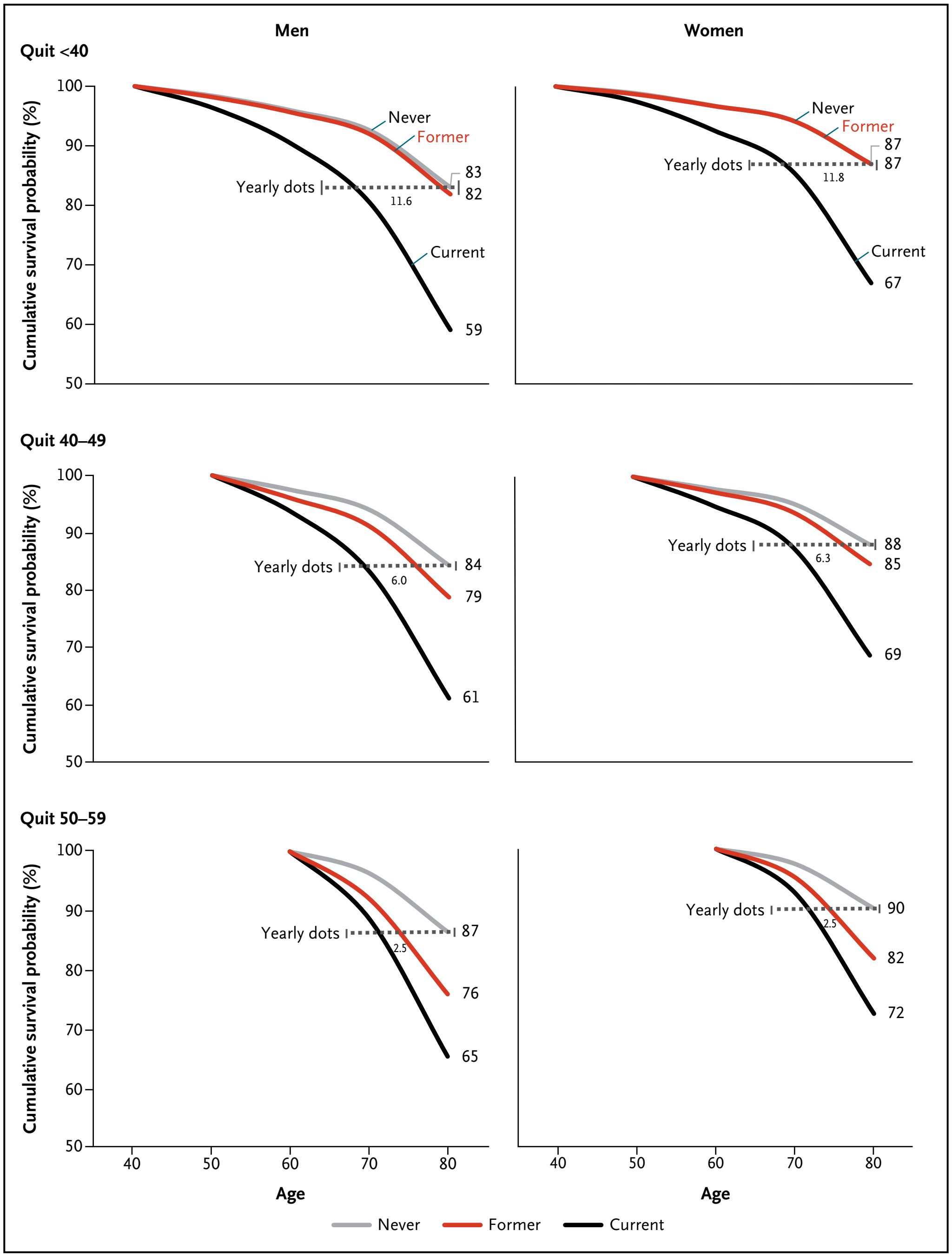

Figure 3. Survival from 40 to 79 Years of Age by Quitting at Various Ages Compared with Never or Current Smokers for All Causes for Men and Women.

meta-analyses may obscure differences among the studies, and we noted heterogeneity in the pooled risks.[23] Finally, the studies might have misclassified death certificates, particularly at older ages.[33,34] Such misclassification should not, however, vary by smoking status. Possible misclassification might raise the current or former smoker:never smoker hazard ratios for some causes but lower it for others.[35] Thus, we focused on deaths by 80 years of age or younger. Finally, misclassification would not affect our current or former smoker:never smoker risk calculations for overall mortality.

Our data support public action to substantially raise cessation rates worldwide given the very large age- and sex-specific benefits of cessation. A simple metric to monitor cessation at the population level is the ratio of former to current smokers approximately 50 years of age.[7] Quitting smoking at any age, particularly in younger years, reduces excess mortality overall and from the major smoking-attributable diseases.[36] These data indicate that quitting smoking is associated with a lower risk of death as early as 3 years after cessation.

Disclosures

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