#### SPECIAL ARTICLE

# 21st-Century Hazards of Smoking and Benefits of Cessation in the United States

Prabhat Jha, M.D., Chinthanie Ramasundarahettige, M.Sc., Victoria Landsman, Ph.D., Brian Rostron, Ph.D., Michael Thun, M.D., Robert N. Anderson, Ph.D., Tim McAfee, M.D., and Richard Peto, F.R.S.

## ABSTRACT

### BACKGROUND

Extrapolation from studies in the 1980s suggests that smoking causes 25% of deaths among women and men 35 to 69 years of age in the United States. Nationally representative measurements of the current risks of smoking and the benefits of cessation at various ages are unavailable.

#### METHODS

We obtained smoking and smoking-cessation histories from 113,752 women and 88,496 men 25 years of age or older who were interviewed between 1997 and 2004 in the U.S. National Health Interview Survey and related these data to the causes of deaths that occurred by December 31, 2006 (8236 deaths in women and 7479 in men). Hazard ratios for death among current smokers, as compared with those who had never smoked, were adjusted for age, educational level, adiposity, and alcohol consumption.

#### RESULTS

For participants who were 25 to 79 years of age, the rate of death from any cause among current smokers was about three times that among those who had never smoked (hazard ratio for women, 3.0; 99% confidence interval [CI], 2.7 to 3.3; hazard ratio for men, 2.8; 99% CI, 2.4 to 3.1). Most of the excess mortality among smokers was due to neoplastic, vascular, respiratory, and other diseases that can be caused by smoking. The probability of surviving from 25 to 79 years of age was about twice as great in those who had never smoked as in current smokers (70% vs. 38% among women and 61% vs. 26% among men). Life expectancy was shortened by more than 10 years among the current smokers, as compared with those who had never smoked. Adults who had quit smoking at 25 to 34, 35 to 44, or 45 to 54 years of age gained about 10, 9, and 6 years of life, respectively, as compared with those who continued to smoke.

#### CONCLUSIONS

Smokers lose at least one decade of life expectancy, as compared with those who have never smoked. Cessation before the age of 40 years reduces the risk of death associated with continued smoking by about 90%.

From the Center for Global Health Research, Toronto (P.J., C.R., V.L.); the Food and Drug Administration, Rockville (B.R.), and the Centers for Disease Control and Prevention, Hyattsville (R.N.A.) - both in Maryland; the American Cancer Society (M.T.) and the Centers for Disease Control and Prevention (T.M.) - both in Atlanta; and the Clinical Trial and Epidemiology Services Unit, University of Oxford, Oxford, United Kingdom (R.P.). Address reprint requests to Dr. Jha at the Center for Global Health Research, St. Michael's Hospital, and Dalla Lana School of Public Health, University of Toronto, Toronto, ON M5C 1N8, Canada.

N Engl J Med 2013;368:341-50. DOI: 10.1056/NEJMsa1211128 Copyright © 2013 Massachusetts Medical Society.

341

The New England Journal of Medicine

Downloaded from nejm.org by MONTSE SALAS VALERO on January 29, 2013. For personal use only. No other uses without permission.

MOKING IS A MAJOR CAUSE OF PREMATURE death worldwide.1-3 Despite substantial declines in the prevalence of smoking by adults, estimates based on extrapolation from studies in the 1980s suggest that for those between 35 and 69 years of age, smoking currently accounts for almost 200,000 deaths annually in the United States, or about one fourth of all deaths in this age group.4-6 The prevalence of smoking peaked around 1960 among U.S. men and about two decades later among U.S. women.7,8 Rates of death from vascular disease have decreased substantially since the 1980s owing to reductions in smoking and in other risk factors and to improved treatment.9 Therefore, extrapolation from previous studies is increasingly uncertain, and direct measurement of the contemporary hazards of smoking in the United States is needed. Moreover, a substantial number of adults have quit smoking in recent decades,8 affording an opportunity to study the effects of cessation at various ages on current mortality.

We report the results of a large, prospective, nationally representative study of smoking and its relation to mortality to provide estimates of the 21st-century hazards of smoking and of the benefits of smoking cessation at various ages for male and female smokers.

#### METHODS

#### STUDY DESIGN

We examined data from a cohort of 216,917 adults in the U.S. National Health Interview Survey (NHIS) between 1997 and 200410-12 that were linked to the National Death Index.13,14 The NHIS is a nationally representative cross-sectional health survey of the civilian, noninstitutionalized population of the United States. The survey uses a stratified, multistage sample design that permits representative sampling of households. One adult (≥18 years of age) is randomly selected from each selected household for a detailed interview on health and other behaviors. The NHIS sample is drawn from each state and the District of Columbia. Each year, approximately 35,000 households and 87,500 persons are newly enrolled in the survey. Black and Hispanic persons are deliberately oversampled, but the sample weights ensure that the final totals conform to national ethnic proportions. The NHIS sampling frame excludes only about 7 million adults (chiefly patients in longterm care facilities, prisoners, and active-duty military personnel) from the total U.S. domestic population of 226 million adults in 2004.<sup>12</sup>

Mortality among survey participants through the end of 2006 was assessed by means of periodic matching of their records to the National Death Index,<sup>13,14</sup> which includes death-certificate information for all deaths in the United States since 1986. Matching was performed for a combination of name, Social Security number, and date of birth, with a success rate exceeding 95%.

Enrollment rates for women exceeded those for men. A total of 122,810 women and 94,107 men 25 years of age or older participated in the NHIS between 1997 and 2004. Of these participants, 9058 women (761 of whom died) and 5611 men (544 of whom died) were excluded because of missing variables (e.g., educational level, smoking status, drinking status, or cause of death).

## STATISTICAL ANALYSIS

Life-threatening illness can cause smokers to quit, which distorts the rates of death among current smokers and among those who have quit smoking recently in opposite ways. Unlike previous analyses of NHIS results,<sup>10,11</sup> our analyses classified former smokers who had quit within 5 years before death as current smokers. Participants were classified as former smokers if they had smoked at least 100 cigarettes in their lifetime but had not smoked within the previous 5 years. Participants were classified as never having smoked if they had smoked fewer than 100 cigarettes in their lifetime.

We calculated hazard ratios for current and former smokers with the use of an age-stratified Cox proportional-hazards model,15 adjusted for educational level (less than high school, high school, or more than high school), alcohol consumption (nondrinker, former drinker, light drinker [1 to 2 drinks per day for women and 1 to 3 drinks per day for men] or moderate-to-heavy drinker [3 or more drinks per day for women and 4 or more drinks per day for men]), and adiposity (a body-mass index [the weight in kilograms divided by the square of the height in meters] of <25, 25.0 to 29.9, or  $\geq$ 30). Further adjustment for race (black, Hispanic, or white) did not materially affect these estimates, and the results of these adjustments are not presented. All estimates were weighted according to the NHIS sample weights.<sup>12</sup>

Since the NHIS death rates are slightly lower than the U.S. national death rates,<sup>13</sup> we scaled

The New England Journal of Medicine

Downloaded from nejm.org by MONTSE SALAS VALERO on January 29, 2013. For personal use only. No other uses without permission.

our estimates of absolute death rates upward to match the U.S. national rates for 2004 by combining smoking prevalence, hazard ratios for smokers versus those who had never smoked, and total deaths, as described previously.<sup>16</sup> From the agespecific death rates among current smokers and those who had never smoked, we calculated the cumulative probabilities of survival from 25 to 79 years of age, with adjustment for differences in age, educational level, alcohol consumption, and adiposity. The absolute differences in mortality between current smokers and those who had never smoked were, however, not materially altered by scaling the death rates (data not shown).

## RESULTS

#### CHARACTERISTICS OF THE STUDY PARTICIPANTS

Current smokers more commonly consumed alcohol, had lower educational levels, and had a lower body-mass index than did former smokers or those who had never smoked (Table 1). About two thirds of current smokers and of former smokers had started smoking before 20 years of age. The proportion of former smokers increased steeply with age (Fig. 1), so that they were, on average, older than current smokers and those who had never smoked. Cessation of smoking was less common among women than among men; the ratio of former smokers to current smokers at 65 to 69 years of age was 2:1 for women but 4:1 for men.

## MORTALITY ACCORDING TO SMOKING STATUS

Among 113,752 women and 88,496 men 25 years of age or older at yearly recruitment, who were followed for a mean of 7 years (1.3 million person-years), a total of 15,715 deaths (8236 deaths in women and 7479 in men) were recorded (see Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org); 10,743 deaths (5122 in women and 5621 in men) occurred at 25 to 79 years of age. The hazard ratios for overall mortality at 25 to 79 years of age among current smokers versus those who had never smoked were 3.0 for women (99% confidence interval [CI], 2.7 to 3.3) and 2.8 for men (99% CI, 2.4 to 3.1) (Table 2). Adjustment for educational level, alcohol consumption, and adiposity had little effect on these age-stratified hazard ratios (data not shown). These age-specific hazard ratios, together with the prevalence of current smoking, were combined with 2004 U.S. death rates to estimate survival from 25 to 79 years of age for current smokers versus those who had never smoked, after adjustment for differences in age, educational level, and adiposity (body-mass index). This analysis showed that a person who had never smoked was about twice as likely as a current smoker to reach 80 years of age (Fig. 2). Among women, the estimated probability of survival to the age of 80 years was 70% (99% CI, 64 to 76) for those who had never smoked but only 38% (99% CI, 30 to 45) for current smokers (Fig. 2A). For men, these probabilities were 61% (99% CI, 55 to 67) for those who had never smoked but only 26% (99% CI, 18 to 33) for current smokers (Fig. 2B). Among current smokers, survival was shorter by about 11 years for women and by about 12 years for men, as compared with participants who had never smoked.

Table 2 shows that much, though not all, of this difference in survival was due to neoplastic disease, vascular disease, or other diseases that previous studies have shown can be caused by smoking.2-6 Notably high hazard ratios were observed for deaths from lung cancer and from ischemic heart disease in both women and men and from stroke in women. However, about 7% of the excess mortality among smokers at 25 to 79 years of age was due to accidents and injuries. In Table 2, only the excess mortality from disease (not from accidents and injuries) is attributed to smoking. At 25 to 79 years of age, about 62% (range, 59 to 65) of all deaths among female smokers and 60% (range, 55 to 63) of all deaths among male smokers would have been avoided if the rates of death from diseases among smokers had been the same as the rates among those who had never smoked and after adjustments for any differences in age, educational level, alcohol consumption, and adiposity.

#### BENEFITS OF SMOKING CESSATION

Hazard ratios for deaths from all causes among former smokers, as compared with those who had never smoked, were similar for women and men and were combined for statistical stability (Table S2 in the Supplementary Appendix). Lung cancer was associated with the highest hazard ratio for death among former smokers (Table S3 in the Supplementary Appendix). The effect of smoking cessation at younger ages was especially favorable (Fig. 3). For smokers who quit at 25 to 34 years of age (median, 29), survival curves were nearly

343

The New England Journal of Medicine

Downloaded from nejm.org by MONTSE SALAS VALERO on January 29, 2013. For personal use only. No other uses without permission.

| Variable  |                   | Women            |                 |                   | Men              |                 |
|---|-------------------|------------------|-----------------|-------------------|------------------|-----------------|
|   | Current<br>Smoker | Former<br>Smoker | Never<br>Smoked | Current<br>Smoker | Former<br>Smoker | Never<br>Smoked |
| No. of participants surveyed  | 23,839            | 22,389           | 67,524          | 23,348            | 25,859           | 39,289          |
| No. of deaths, according to cause†  |                   |                  |                 |                   |                  |                 |
| All causes  | 1798              | 2070             | 4368            | 2174              | 3335             | 1970            |
| Lung cancer   | 289               | 163              | 83              | 362               | 274              | 52              |
| All cancers   | 572               | 518              | 875             | 696               | 901              | 440             |
| Vascular diseases   | 571               | 742              | 1978            | 698               | 1304             | 840             |
| Respiratory diseases  | 248               | 276              | 272             | 222               | 385              | 105             |
| No. of all-cause deaths at ages 25 to 79 yr   | 1579              | 1353             | 2190            | 2030              | 2308             | 1283            |
| Mean age — yr   | 45.8              | 55.3             | 50.1            | 45.0              | 56.9             | 45.7            |
| Educational level — no. of participants (%)‡  |                   |                  |                 |                   |                  |                 |
| <high-school graduate<="" td=""><td>5,438 (31.3)</td><td>3,968 (13.8)</td><td>14,675 (55.0)</td><td>5,835 (41.2)</td><td>5,643 (23.1)</td><td>6,145 (35.8)</td></high-school> | 5,438 (31.3)      | 3,968 (13.8)     | 14,675 (55.0)   | 5,835 (41.2)      | 5,643 (23.1)     | 6,145 (35.8)    |
| High-school graduate  | 8,532 (29.2)      | 6,625 (18.2)     | 18,670 (52.6)   | 8,157 (34.4)      | 7,389 (26.1)     | 9,710 (39.5)    |
| >High-school graduate   | 9,869 (17.0)      | 11,796 (21.5)    | 34,179 (61.5)   | 9,356 (19.8)      | 12,827 (26.3)    | 23,434 (53.9)   |
| Alcohol consumption — no. of participants (%);  |                   |                  |                 |                   |                  |                 |
| Nondrinker  | 3,388 (11.5)      | 3,158 (7.4)      | 27,303 (81.0)   | 1,522 (13.9)      | 1,894 (11.7)     | 8,323 (74.5)    |
| Former drinker  | 4,328 (25.8)      | 5,367 (25.3)     | 8,877 (48.9)    | 3,788 (27.8)      | 6,925 (33.3)     | 4,977 (38.9)    |
| Light drinker∬  | 10,410 (20.7)     |                  | 27,364 (56.1)   |                   | 14,272 (27.3)    | 21,486 (48.2)   |
| Moderate-to-heavy drinker¶  | 5,713 (46.8)      | 2,096 (22.7)     | 3,980 (30.5)    | 6,542 (47.0)      | 2,768 (23.8)     | 4,503 (29.2)    |
| Body-mass index — no. of participants (%)‡  |                   |                  |                 |                   |                  |                 |
| <24   | 12,343 (24.4)     | 9,796 (18.7)     | 30,965 (56.9)   | 9,137 (34.4)      | 6,988 (20.9)     | 12,023 (44.7    |
| 25–29   | 6,549 (22.0)      | 6,727 (18.7)     | 20,158 (59.3)   | 9,744 (25.0)      | 12,194 (26.8)    | 18,236 (48.2)   |
| ≥30   | 4,947 (19.6)      | 5,866 (20.7)     | 16,401 (59.7)   | 4,467 (22.9)      | 6,677 (29.3)     | 9,030 (47.8     |
| Race — no. of participants (%)‡**   | . ,               |                  |                 |                   | . ,              |                 |
| White   | 17,075 (24.5)     | 17,647 (21.8)    | 40,972 (53.7)   | 15,972 (27.6)     | 19,952 (27.2)    | 25,498 (45.2)   |
| Nonwhite  | 6,764 (17.3)      | 4,742 (12.3)     | 26,552 (70.4)   | 7,376 (26.7)      | 5,907 (21.2)     | 13,791 (52.2)   |
| Age when participant started smoking — no.<br>of participants (%)††   |                   |                  |                 |                   |                  |                 |
| <20 yr  | 15,726 (67.8)     | 14,330 (66.4)    |                 | 16,925 (73.5)     | 19,431 (75.5)    |                 |
| 20–24 yr  | 4,592 (18.9)      | 4,370 (18.8)     |                 | 4,092 (17.2)      | 4,042 (15.5)     |                 |
| ≥25 yr  | 3,521 (13.2)      | 3,689 (14.8)     |                 | 2,331 (9.3)       | 2,386 (9.0)      |                 |
| Cigarettes smoked per day — no.<br>of participants (%)††  |                   |                  |                 |                   |                  |                 |
| <10   | 6,865 (26.1)      |                  |                 | 5,592 (22.0)      |                  |                 |
| 10–19   | 7,223 (30.9)      |                  |                 | 5,502 (23.6)      |                  |                 |
| ≥20   | 9,393 (41.6)      |                  |                 | 11,831 (52.7)     |                  |                 |
| Missing data  | 358 (1.4)         |                  |                 | 423 (1.7)         |                  |                 |

\* Women and men who were 25 years of age or older were included in the study cohort. This analysis excluded 5611 men (5%) and 9058 women (7%) for whom data on educational level, alcohol consumption, body-mass index, race, or smoking status were missing.

These constituted deaths that occurred up to December 31, 2006. The International Classification of Diseases, 10th revision, codes were C33–34 for lung cancer, C00–97 for all cancers, 100–99 for vascular diseases, and J00–99 for respiratory diseases.

Prevalence (expressed as percentages in parentheses) was weighted by the NHIS survey weights and standardized to the age distribution of current smokers for men and for women.

Light drinking was defined as 1 to 2 drinks per day for women and 1 to 3 drinks per day for men.

🖣 Moderate-to-heavy drinking was defined as 3 or more drinks per day for women and 4 or more drinks per day for men.

The body-mass index is the weight in kilograms divided by the square of the height in meters.

\*\* Race was self-reported.

†† Column proportions were weighted by the NHIS survey weights.

N ENGLJ MED 368;4 NEJM.ORG JANUARY 24, 2013

The New England Journal of Medicine

Downloaded from nejm.org by MONTSE SALAS VALERO on January 29, 2013. For personal use only. No other uses without permission.

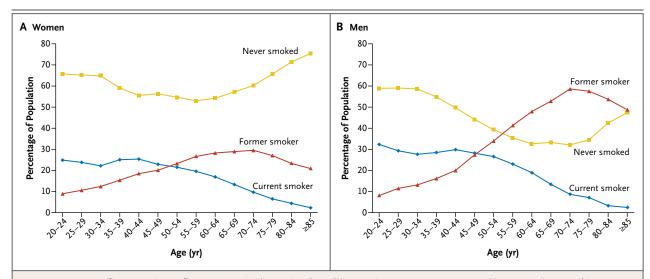


Figure 1. Age-Specific Proportions of Participants in the National Health Interview Survey (NHIS) According to Baseline Smoking Status, 1997–2004.

The proportions of NHIS participants who were current smokers, former smokers, and those who never smoked are shown for women (Panel A) and for men (Panel B).

identical to those for participants who had never smoked, meaning that those who quit smoking gained about 10 years of life, as compared with those who continued to smoke. Survival curves were somewhat worse for smokers who had quit at 35 to 44 years of age (median, 39) than for those who had never smoked; still, smokers who quit smoking could expect to gain about 9 years of life, as compared with those who continued to smoke. Thus, cessation at about 39 years of age reduced the excess risk of death from any cause by about 90%. Nevertheless, smokers who had quit by about 39 years of age still had a 20% excess risk (hazard ratio, 1.2), as compared with those who had never smoked. Although this hazard is substantial, it is much smaller than the 200% excess risk (hazard ratio, 3.0) among those who continued to smoke (Fig. 4).

Smokers who stopped smoking at 45 to 54 years of age and those who stopped at 55 to 64 years of age (median, 49 and 59 years, respectively) gained about 6 and 4 years of life, respectively. Even cessation at the age of 45 to 54 years reduced the excess risk of death by about two thirds. Since some of the smokers who died might have quit smoking as a result of the disease that eventually killed them, the hazard ratios for former smokers might be biased upward (and the benefits of cessation might be even greater than shown). Exclusion of the first few years of follow-up would help limit this "reverse causality," but when we excluded the first 2 years of follow-up from the analysis, the results were similar (data not shown).

## DISCUSSION

The overall mortality among smokers of both sexes in the United States is about three times as high as that among otherwise similar persons who never smoked, and the smokers lose, on average, at least a decade of life. The women in this cohort represent the first generation of women in the United States in which those who smoked began early in life and smoked for decades, and the risks of death for these women are about 50% greater than the risks reported in the 1980s studies.4,5 For both female and male smokers, the tripling of the relative risk of death and the reduction in survival by at least a decade are similar to the risks in four other studies: a study of male British doctors born between 1900 and 1930,17,18 the large U.K. study of women born between 1930 and 1950,19 a meta-analysis of several other U.S. cohort studies,<sup>20</sup> and a study in Japan of people born between 1920 and 1945.21 Although the relative risks were similarly tripled across the studies, the absolute death rates (for both current smokers and those who had never smoked) were much higher in our study than in other U.S. studies,20 since the NHIS is more representative of

345

The New England Journal of Medicine

Downloaded from nejm.org by MONTSE SALAS VALERO on January 29, 2013. For personal use only. No other uses without permission.

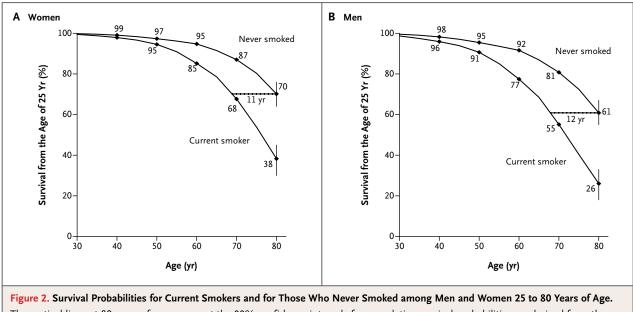
| Table 2. Adjusted Hazard Ratios for Various Causes  | s of Death am   | ong Current                             | Smokers, as Comp  | of Death among Current Smokers, as Compared with Those Who Never Smoked, among Women and Men 25 to 79 Years of Age. $st$ | ever Smoked,                   | among Wom                        | en and Men 25 to                     | 79 Years of Age.*                                  |
|---|---|---|---|--|--------------------------------|----------------------------------|--------------------------------------|--|
| Cause of Death  |   |   | Women   |  |                                |                                  | Men                                  |  |
|   | Never<br>Smoked   | Current<br>Smoker                       | Adjusted<br>Hazard Ratio<br>(99% CI)                      | Deaths Attributable<br>to Smoking among<br>Smokers   | Never<br>Smoked                | Current<br>Smokers               | Adjusted<br>Hazard Ratio<br>(99% CI) | Deaths Attributable<br>to Smoking among<br>Smokers |
|   | no. of deaths   | teaths                                  |   | no. (%)  | no. of                         | no. of deaths                    |                                      | no. (%)  |
| Lung cancer   | 61  | 267                                     | 17.8 (11.4–27.8)  | 252 (94)   | 44                             | 348                              | 14.6 (9.1–23.4)                      | 324 (93)   |
| Cancers other than lung cancer  | 544   | 258                                     | 1.7 (1.4–2.1)   | 106 (41)   | 280                            | 317                              | 2.2 (1.7–2.8)                        | 173 (55)   |
| All cancers   | 605   | 525                                     | 3.2 (2.6–3.9)   | 360 (69)   | 324                            | 665                              | 3.8 (3.1–4.8)                        | 491 (74)   |
| Ischemic heart disease  | 382   | 251                                     | 3.5 (2.7–4.6)   | 179 (72)   | 285                            | 416                              | 3.2 (2.5–4.1)                        | 288 (69)   |
| Stroke  | 150   | 88                                      | 3.2 (2.2–4.7)   | 60 (69)  | 74                             | 99                               | 1.7 (1.0–2.8)                        | 27 (40)  |
| Other vascular disease  | 252   | 137                                     | 3.1 (2.2–4.4)   | 93 (68)  | 141                            | 161                              | 2.1 (1.5–3.0)                        | 84 (52)  |
| All vascular diseases   | 784   | 476                                     | 3.2 (2.7–3.9)   | 328 (69)   | 500                            | 643                              | 2.6 (2.1–3.2)                        | 395 (61)   |
| Respiratory diseases  | 119   | 206                                     | 8.5 (6.1–11.8)  | 182 (88)   | 45                             | 188                              | 9.0 (5.6–14.4)                       | 167 (89)   |
| Other medical disorders not shown above   | 581   | 277                                     | 2.2 (1.7–2.8)   | 151 (55)   | 295                            | 370                              | 2.2 (1.7–2.9)                        | 205 (55)   |
| All medical disorders   | 2089  | 1484                                    | 3.0 (2.7–3.3)   | 986 (66)   | 1164                           | 1866                             | 2.9 (2.5–3.2)                        | 1211 (65)  |
| Accidents and injuries  | 101   | 95                                      | 3.9 (2.4–6.2)   | 0  | 119                            | 164                              | 2.1 (1.4–3.0)                        | 0  |
| All causes†   | 2190  | 1579                                    | 3.0 (2.7–3.3)   | 986 (62)   | 1283                           | 2030                             | 2.8 (2.4–3.1)                        | 1211 (60)  |
| * Hazard ratios were adjusted for age, educational level, alcohol consumption, and body-mass index.<br>† Deaths attributable to smoking were determined with the use of the hazard ratios for all medical causes of death. With the exclusion of the 199 women and 222 men who had quit<br>smoking less than 5 years before their deaths and the exclusion of the 1795 women and 2184 men who reported a history of coronary heart disease, stroke, or cancer, the hazard ratios<br>for all-cause mortality were 3.1 for women and 2.8 for men. | evel, alcohol c<br>vith the use of<br>the exclusion<br>for men. | onsumption<br>the hazard<br>of the 1795 | , and body-mass i<br>atios for all medi<br>women and 2184 | ndex.<br>cal causes of death. With<br>men who reported a hist  | the exclusior<br>ory of corona | n of the 199 v<br>ry heart disea | omen and 222 m<br>se, stroke, or can | en who had quit<br>cer, the hazard ratios          |

## The NEW ENGLAND JOURNAL of MEDICINE

N ENGLJ MED 368;4 NEJM.ORG JANUARY 24, 2013

The New England Journal of Medicine

Downloaded from nejm.org by MONTSE SALAS VALERO on January 29, 2013. For personal use only. No other uses without permission.



The vertical lines at 80 years of age represent the 99% confidence intervals for cumulative survival probabilities, as derived from the standard errors estimated with the use of the jackknife procedure. Survival probabilities have been scaled from the National Health Interview Survey to the U.S. rates of death from all causes at these ages for 2004,<sup>13,16</sup> with adjustment for differences in age, educational level, alcohol consumption, and adiposity (body-mass index).

the general U.S. population. Thus, in the NHIS, the large absolute differences in risk between current smokers and those who never smoked, as well as the gains in years of life for those who quit smoking, are likely to be true for the U.S. population as a whole. The hazards associated with smoking are substantial, even though in recent decades, most smokers in the United States have smoked cigarettes with relatively low levels of tar, as measured by machine testing, as compared with the cigarettes smoked in earlier decades.<sup>22</sup>

Twenty-first-century measurement of the hazards of tobacco use must take into account the substantial reductions in mortality from vascular diseases and in overall mortality since 1970.<sup>5,9,23</sup> As death rates among those who never smoked have fallen, the absolute differences in survival to the age of 80 years between those who continue to smoke and those who have never smoked have widened and now exceed 30% for both sexes. Moreover, the hazards among women who continue to smoke now approximate those among male smokers,<sup>10,11,20,21</sup> at least in middle age.

Because the absolute risks of continuing to smoke are large, the absolute benefits of cessation will also be large, particularly as death rates among those who have never smoked continue to fall.<sup>24</sup> Cessation at around 40 years of age results in approximately a 90% reduction in the excess risk of death associated with continued smoking in later middle age and old age. That is not to say, however, that it is safe to smoke until 40 years of age and then stop, for the remaining excess risk of about 20% (hazard ratio, 1.2) is substantial; it means that about one in six of these former smokers who dies before the age of 80 years would not have died if their death rates had been similar to those for persons who had never smoked who were similar in educational levels, adiposity, and alcohol use.

From 1965 to 2010, the prevalence of cigarette smoking among adults in the United States decreased from 42% to 19%, owing in large part to increased rates of cessation.<sup>8</sup> Although former smokers still far outnumber current smokers at older ages (and especially among men) (Fig. 1), the United States has about 35 million current or future smokers under 35 years of age,<sup>25</sup> and the prevalence of smoking changed little from 2004 to 2010.<sup>8</sup>

Our study has some limitations. First, there may be confounding factors other than the few variables recorded in the NHIS. However, most

347

The New England Journal of Medicine

Downloaded from nejm.org by MONTSE SALAS VALERO on January 29, 2013. For personal use only. No other uses without permission.

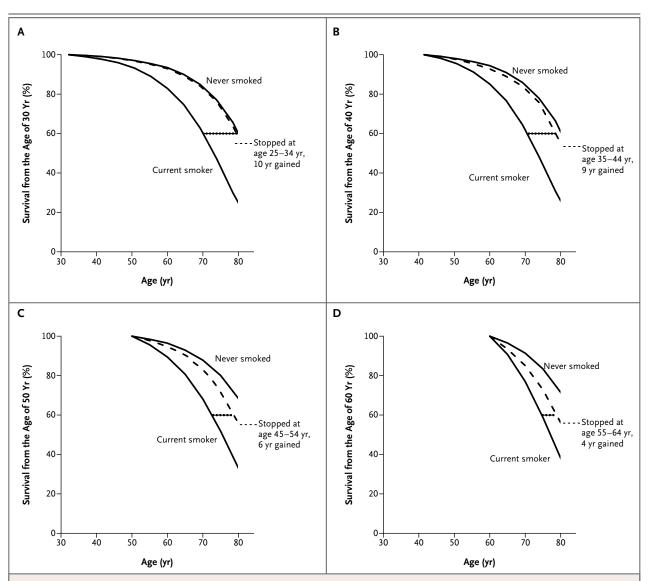


Figure 3. Effect of Smoking Cessation on Survival to 80 Years of Age, According to Age at the Time of Quitting.

Life expectancy was increased from 4 to 10 years among smokers who quit, depending on their age at the time of smoking cessation. Panel A shows the effect of quitting at 25 to 34 years of age (effect shown from the age of 30), Panel B the effect of quitting at 35 to 44 years of age (effect shown from the age of 40), Panel C the effect of quitting at 45 to 54 years of age (effect shown from the age of 50), and Panel D the effect of quitting at 55 to 64 years of age (effect shown from the age of 60). Survival probabilities have been scaled from the NHIS to the U.S. rates of death from all causes at these ages for 2004,<sup>13,16</sup> with adjustment for differences in age, educational level, alcohol consumption, and adiposity (body-mass index). The horizontal dots represent years of life gained.

> of the excess mortality among smokers was from neoplastic, vascular, or respiratory diseases that other studies have shown can be caused by smoking,<sup>2-6</sup> and adjustment for educational level, alcohol use, and adiposity did little to alter the hazard ratios, suggesting that, to a large degree, the association between smoking and mortality is causal. Second, the NHIS excludes incarcer-

ated adults (who tend to have an increased prevalence of smoking<sup>26</sup>). This should not, however, materially affect the observed differences between current smokers and those who never smoked, among the adults surveyed in the NHIS. Third, the number of deaths in the NHIS was lower than that noted in recent studies,<sup>19,20</sup> but this is counterbalanced by the fact that the sur-

N ENGLJ MED 368;4 NEJM.ORG JANUARY 24, 2013

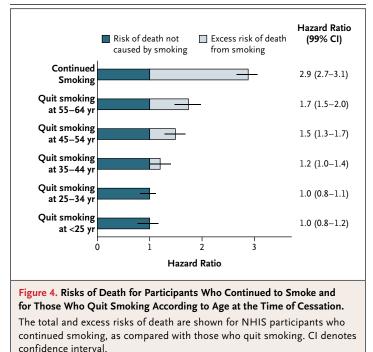
The New England Journal of Medicine

Downloaded from nejm.org by MONTSE SALAS VALERO on January 29, 2013. For personal use only. No other uses without permission.

veyed population and death rates in our study are generally representative of the U.S. population and death rates.13 Fourth, misclassification of the causes of death, particularly at older ages, might affect the observed hazards for some causes of death (lowering the risks for some causes but raising the risks for others), but this would not affect our analyses of all-cause mortality. Fifth, the NHIS is a cross-sectional survey, and data on smoking status were collected only at baseline. Some of the surveyed smokers would have quit subsequently, thereby somewhat reducing their risk,8 but with 7 years of follow-up, any distortion of the hazard ratios should be slight. Similarly, the excess mortality among former smokers might be overestimated, since some deaths may well reflect deaths among smokers who quit because they became ill. In this case, the true gain of life-years from the time of cessation would be somewhat greater than we estimated. Finally, although the smokers who quit smoking might have been more likely than those who had never smoked to try to improve their health, we found little difference between these two groups with respect to alcohol use, adiposity, and other healthrelated variables.

Our findings, as well as those from other recent prospective studies,19-21 highlight the worldwide importance of tobacco control. About 40 million Americans smoke, but most of the world's estimated 1.3 billion smokers live in lowand middle-income countries.<sup>3,25</sup> Worldwide, about 30 million young adults begin smoking each year (about 50% of young men and about 10% of young women), and current patterns of behavior suggest that most will not stop.25 Our findings are consistent with emerging evidence from China<sup>27</sup> and India<sup>16</sup> that cigarette smokers worldwide who continue to smoke can expect to lose about a decade of life.3-5 In most highincome countries, there are now more former smokers than current smokers; however, cessation remains uncommon in low- and middleincome countries.<sup>3,25</sup> Thus, on the basis of current rates of smoking initiation and cessation, smoking, which killed about 100 million people in the 20th century, will kill about 1 billion in the 21st century.<sup>1,3,5,24</sup>

Options to help increase cessation rates and decrease initiation rates worldwide include higher prices for cigarettes through an increased ex-



cise tax, restrictions on smoking in public places, bans on tobacco advertising and promotion, public education about the hazards of smoking and the benefits of cessation, and easy access to cessation efforts.<sup>3,28</sup> In the United States, the recent increase of 62 cents in the federal excise tax on each pack of cigarettes,29 a recent federal massmedia campaign,30 and the extension of insurance coverage for cessation as part of the Affordable Care Act are likely to raise cessation rates. A focus on cessation of smoking is justified, since quitting smoking before the age of 40 years, and preferably much earlier, will reduce by about 90% the decade of life that is lost from continued smoking. Smoking is associated with a decade of lost life, and cessation reduces that loss by about 90%.

The opinions expressed in this article are those of the authors and do not necessarily represent the opinions of the agencies at which the authors are employed.

Supported by a grant (TW007939-01) from the Fogarty International Center, National Institutes of Health; by a grant (IEG-53506) from the Canadian Institutes of Health Research; and by the Disease Control Priorities Project, Bill and Melinda Gates Foundation. Dr. Jha holds an endowed faculty position at the University of Toronto.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Samira Asma, Tom Frieden, Howard Hu, and Arthur Slutsky for useful comments and Jennifer Parker for assistance with the NHIS data.

The New England Journal of Medicine

Downloaded from nejm.org by MONTSE SALAS VALERO on January 29, 2013. For personal use only. No other uses without permission.

#### REFERENCES

**1.** MPOWER: a policy package to reverse the tobacco epidemic. Geneva: World Health Organization, 2011.

**2.** Tobacco smoke and involuntary smoking: IARC monographs on the evaluation of carcinogenic risks to humans. Vol. 83. Lyon, France: International Agency for Research on Cancer, 2004.

**3.** Jha P. Avoidable global cancer deaths and total deaths from smoking. Nat Rev Cancer 2009;9:655-64.

4. Peto R, Lopez AD, Boreham J, Thun M, Heath C Jr. Mortality from smoking in developed countries, 1950–2000. Oxford, United Kingdom: Oxford University Press, 1994.

5. Peto R, Lopez AD, Boreham J, Thun M. Mortality from smoking in developed countries, 1950–2005. 2nd ed. (http://www.ctsu.ox.ac.uk/~tobacco).

**6.** Department of Health and Human Services. The health consequences of smoking: a report of the Surgeon General. Washington, DC: Government Printing Office, 2004.

 Forey B, Hamling J, Hamling J, Thornton A, Lee P. International smoking statistics 2006-2012. Oxford, United Kingdom: Oxford University Press, 2002.
 Quitting smoking among adults — United States, 2001–2010. MMWR Morb Mortal Wkly Rep 2011;60:44-9.

9. Prevalence of coronary heart disease
— United States, 2006–2010. MMWR
Morb Mortal Wkly Rep 2011;60:1377-81.
10. Rostron B. Smoking-attributable mortality in the United States. Epidemiology
2011;22:350-5.

**11.** Mehta N, Preston S. Continued increases in the relative risk of death from smoking. Am J Public Health 2012;102: 281-6.

12. National Health Interview Survey. Hyattsville, MD: National Center for Health Statistics, June 2010 (http://www .cdc.gov/nchs/nhis.htm).

**13.** Ingram DD, Lochner KA, Cox CS. Mortality experience of the 1986–2000 National Health Interview Survey Linked Mortality Files participants. Vital Health Stat 2008:147:1-37.

14. National Health Interview Survey (1986-2004) Linked Mortality Files, mortality follow-up through 2006: matching methodology. Hyattsville, MD: National Center for Health Statistics, May 2009

(http://www.cdc.gov/nchs/data/ datalinkage/matching\_methodology\_

nhis\_final.pdf).

**15.** Pencina MJ, Larson MG, D'Agostino RB. Choice of time scale and its effect on significance of predictors in longitudinal studies. Stat Med 2007;26:1343-59.

**16.** Jha P, Jacob B, Gajalakshmi V, et al. A nationally representative case–control study of smoking and death in India. N Engl J Med 2008;358:1137-47.

**17.** Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ 2004;328:1519-33.

18. Peto R, Beral V. Sir Richard Doll CH OBE: 28 October 1912–24 July 2005. Biogr Mems Fell R Soc 2010;56:63-83 (http:// rsbm.royalsocietypublishing.org/ content/56/63.full.pdf+html).

**19.** Pirie K, Peto R, Reeves GK, Green J, Beral V. The 21st century hazards of smoking and benefits of stopping: a prospective study of one million women in the UK. Lancet 2012 October 26 (Epub ahead of print).

**20.** Thun MJ, Carter BD, Feskanich D, et al. 50-Year trends in smoking-related deaths in the United States. N Engl J Med 2013;368:361-74.

**21.** Sakata R, McGale P, Grant EJ, Ozasa K, Peto R, Darby SC. Impact of smoking

on mortality and life expectancy in Japanese smokers: a prospective cohort study. BMJ 2012;345:e7903.

**22.** Hoffmann D, Hoffmann I. The changing cigarette, 1950-1995. J Toxicol Environ Health 1997;50:307-64.

**23.** Thun M, Peto R, Boreham J, Lopez AD. Stages of the cigarette epidemic on entering its second century. Tob Control 2012;21:96-101.

24. The hazards of smoking and the benefits of stopping. In: Tobacco control: reversal of risk after quitting smoking. IARC handbooks of cancer prevention, Vol. 11. Lyon, France: International Agency for Research on Cancer, 2007:15-27.

**25.** Giovino GA, Mirza SA, Samet JM, et al. Tobacco use in 3 billion individuals from 16 countries: an analysis of nationally representative cross-sectional house-hold surveys. Lancet 2012;380:668-79.

**26.** Ritter C, Stöver H, Levy M, Etter JF, Elger B. Smoking in prisons: the need for effective and acceptable interventions. J Public Health Policy 2011;32:32-45.

**27.** Peto R, Chen ZM, Boreham J. Tobacco — the growing epidemic. Nat Med 1999;5:15-7.

**28.** Jha P, Chaloupka FJ. Curbing the epidemic: governments and the economics of tobacco control. Washington, DC: World Bank, 1999.

**29.** Baumgardner JR, Bilheimer LT, Booth MB, Carrington WJ, Duchovny NJ, Werble EC. Cigarette taxes and the federal budget — report from the CBO. N Engl J Med 2012;367:2068-70.

**30.** Rigotti N, Wakefield M. Real people, real stories: a new mass media campaign that could help smokers quit. Ann Intern Med 2012 September 25 (Epub ahead of print).

Copyright © 2013 Massachusetts Medical Society.

#### AN NEJM APP FOR IPHONE

The NEJM Image Challenge app brings a popular online feature to the smartphone. Optimized for viewing on the iPhone and iPod Touch, the Image Challenge app lets you test your diagnostic skills anytime, anywhere. The Image Challenge app randomly selects from 300 challenging clinical photos published in NEJM, with a new image added each week. View an image, choose your answer, get immediate feedback, and see how others answered. The Image Challenge app is available at the iTunes App Store.

The New England Journal of Medicine

Downloaded from nejm.org by MONTSE SALAS VALERO on January 29, 2013. For personal use only. No other uses without permission.