Introduction, Summary, and Conclusions

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Cigarette smoking is the largest preventable cause of death and disability in developed countries and is a rapidly growing health problem in developing countries. The magnitude and nature of the risks associated with smoking can be estimated using data from prospective epidemiological studies of smokers and nonsmokers and information on smoking in the population. In 1966 the National Cancer Institute (NCI) published the monograph *Epidemiological Approaches to the Study of Cancer and Other Chronic Diseases* (Haenszel, 1966), which included detailed presentations of the information available up to that time from several large prospective mortality studies examining relationships between smoking behavior and disease. Since then, several new large prospective mortality studies have been initiated, and additional years of followup are available for analysis for some of the studies whose results were presented in 1966. This new information can be used to more sharply characterize the risks of smoking.

The goal of this monograph is to provide detailed presentations of disease risks caused by smoking using data from these more recent studies and the more extensive followup data available from the American Cancer Society (ACS) Cancer Prevention Study I (CPS-I). This volume also contains descriptions of the quantitative relationships between various aspects of smoking behavior and disease occurrence as well as detailed tabular data contained in various chapter appendixes. Appendix data are presented in greater detail than would be required by most readers to facilitate use of this volume as a resource by investigators attempting to model or control for the effects of smoking in other epidemiological studies.

Five major prospective epidemiological studies are featured in this volume. CPS-I and CPS-II each followed more than 1 million individuals, with findings on followup of 6 years for CPS-II and 12 years for CPS-I reported in this volume. Because these two studies were initiated more than 20 years apart, they afford the opportunity to examine changes in mortality risks for smokers and nonsmokers incomparable populations over time; the mortality experiences during the first 6 years of followup for both studies are compared in Chapter 4 of this volume.

The Dorn study of U.S. veterans (Kahn, 1966) has the longest duration of followup of the prospective mortality studies, but it lacks repeat measures of smoking status during the followup period. It groups smokers who continued to smoke during followup and those who quit during the followup interval. Because of this limitation, analyses of this study are most informative for disease risks after prolonged periods of abstinence from smoking (Chapter 7). The mortality experience after 26 years of followup of veterans who were former smokers at the start of the study is used to describe the magnitude of disease risks in former smokers compared to lifelong never-smokers.

The Kaiser Permanente Prospective Mortality study (Chapter 6) followed 60,000 individuals enrolled in the Kaiser Permanente Health Plan and included a large proportion of Asian and African-American participants. The Nurses' Health Study (Chapter 8) enrolled 121,700 female registered nurses in 1976 and provides detailed risk estimates for these females, particularly those of younger and middle age.

Detailed estimates of the changes in smoking status with age and calendar year for white and black males and females by 5-year birth cohorts also are presented (Chapter 2).

Considerable effort was made to standardize the presentation of data among the studies, but significant differences exist in ascertainment of smoking status and in reporting of duration of smoking in the analyses. All the analyses accrued deaths and person-years of observation (PYO's) into age groups defined by age of the subject at death or in the year of followup (age was advanced during followup) and assumed that smoking status remained unchanged from the last followup measure of smoking status (CPS-I [Chapter 3] and the Nurses' Health Study) or from entry into the study (CPS-II [Chapter 5], Kaiser Permanente, and veterans studies). Analyses of the American Cancer Society CPS-I and the Kaiser Permanente study accrued deaths and PYO's into duration-of-smoking groups defined by duration of smoking at death or at the year of followup (duration was advanced during followup), but only CPS-I had questionnaire validation of smoking status during followup. Analyses of CPS-II accrued deaths and PYO's into duration-of-smoking groups defined by duration of smoking at entry into the study (duration was not advanced during followup). The study of U.S. veterans (Chapter 7) and the Nurses' Health Study do not present analyses by duration of smoking.

Understanding the impact of cigarette smoking on disease occurrence requires estimates of both the risks and prevalence rates of smoking. This volume provides descriptions of smoking behavior over time during the past century as well as disease-specific mortality estimates from several large prospective mortality studies. The goal is to provide, in one volume, as much information as possible on smoking and mortality to facilitate understanding of smoking-induced disease.

TRENDS IN SMOKING PREVALENCE

Cigarette smoking as a form of tobacco use has largely been a 20th century phenomenon. Before 1910 almost all tobacco was consumed in pipes and cigars or as chewing tobacco and snuff. Beginning in 1913 mass marketing efforts of Camel and other cigarette brands were followed by a rapid rise in the number of cigarettes sold. Cigarette smoking was predominantly a male behavior at that time, and among males, it increased dramatically during and subsequent to World War I. Smoking was relatively uncommon behavior among females until the 1930's. The increase in smoking among females also coincided with a major national advertising campaign. Lucky Strike's "Reach for a Lucky Instead of a Sweet" campaign was one of the first tobacco advertising campaign to directly target females.

The prevalence of current smoking among sequential 5-year birth cohorts of white males and white females is presented in Figures 1 and 2, respectively. A birth cohort consists of all individuals born during specific calendar years, and birth cohort analyses present the experience of those individuals as they age. Birth cohort analyses are presented in Figures 1 and 2 for 5-year birth cohorts of white males and females born between 1885 and 1969.

Differences in smoking behavior over time explain many of the differences in U.S. lung cancer death rates among white and black males and females. Lung cancer had been a rare disease at the turn of the century, but lung cancer death rates rose rapidly among males beginning in the 1930's, about 20 to 25 years after the upsurge of cigarette smoking among males. Figure 3 presents race- and gender-specific, age-adjusted U.S. lung cancer death rates for the calendar years 1950 to 1993. Male lung cancer rates continued to rise into the 1980's, whereas female lung cancer death rates began to increase sharply only in the late 1960's. A major reason for the temporal differences between male and female lung cancer rates relates to the differences in smoking behavior presented in Figures 1 and 2. Females did not initiate smoking in large numbers until the 1930's, 20 to 25 years after the upswing in prevalence among males. As expected, female lung cancer death rates did not begin to increase steeply until the late 1960's, about 20 to 30 years after the beginning of rapid increases in male lung cancer death rates.

Peak rates of smoking prevalence were much higher among males earlier in this century, consistent with the higher lung cancer rates among males across the country. Prevalence rates of smoking in all birth cohorts among white males have been declining since the late 1950's (Figure 1), which is probably the major reason for the leveling off and subsequent decline in male lung cancer death rates evident during the late 1980's (Figure 3) (20 to 25 years after cessation).

Black males born before 1915 and black females born before 1920 had lower rates of smoking initiation than white males and females. Blacks born later in the century had rates of smoking that equaled or exceeded those of whites. Current smoking prevalence among black males is substantially higher than among white males, reflecting both higher rates of initiation and lower rates of cessation.

Comparison of smoking prevalence rates for birth cohorts of white and black males shows a similar relationship between differences in smoking behavior and differences in white and black lung cancer death rates. Before 1950 most cohorts of white males had higher lung cancer rates than the comparable cohorts of black males. By 1965 the pattern had inverted, with most cohorts of white males having lower lung cancer rates than the comparable cohorts of black males. The expected differences between white and black male lung cancer death rates are evident in Figure 3. Before 1960 white male lung cancer death rates exceeded those for black males, but by the mid-1960's lung cancer death rates among black males began to exceed those for white males, and they are currently dramatically higher among black males.

Figure 1
Prevalence of current cigarette smoking by 5-year birth cohorts of white males

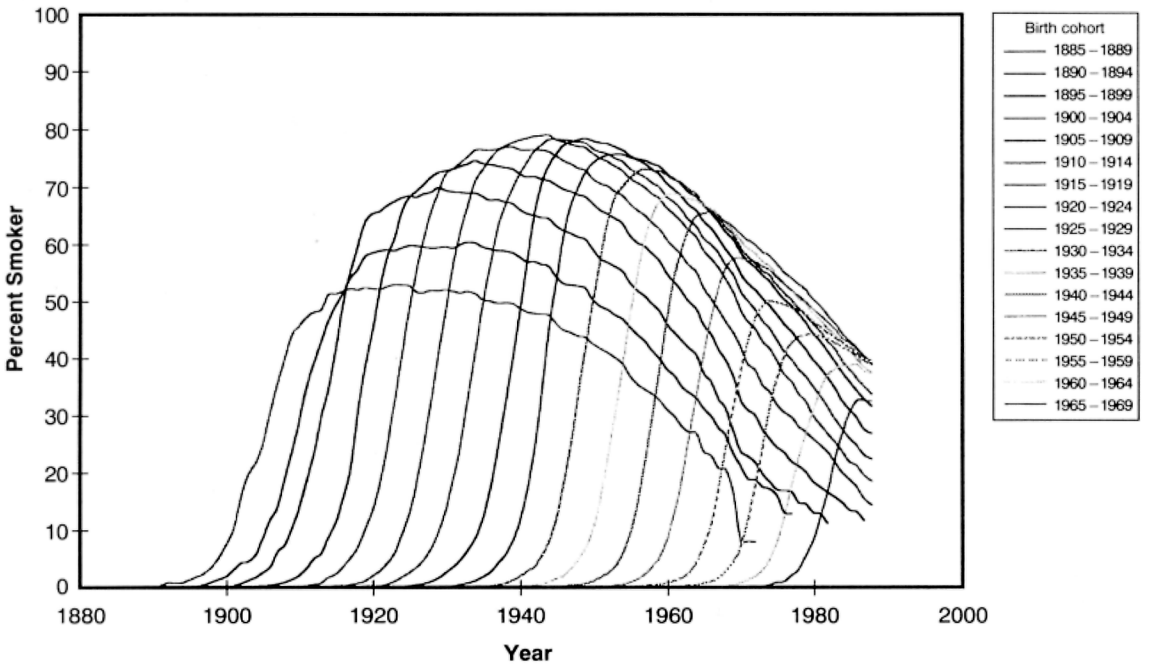


Figure 2
Prevalence of current cigarette smoking by 5-year birth cohorts of white females

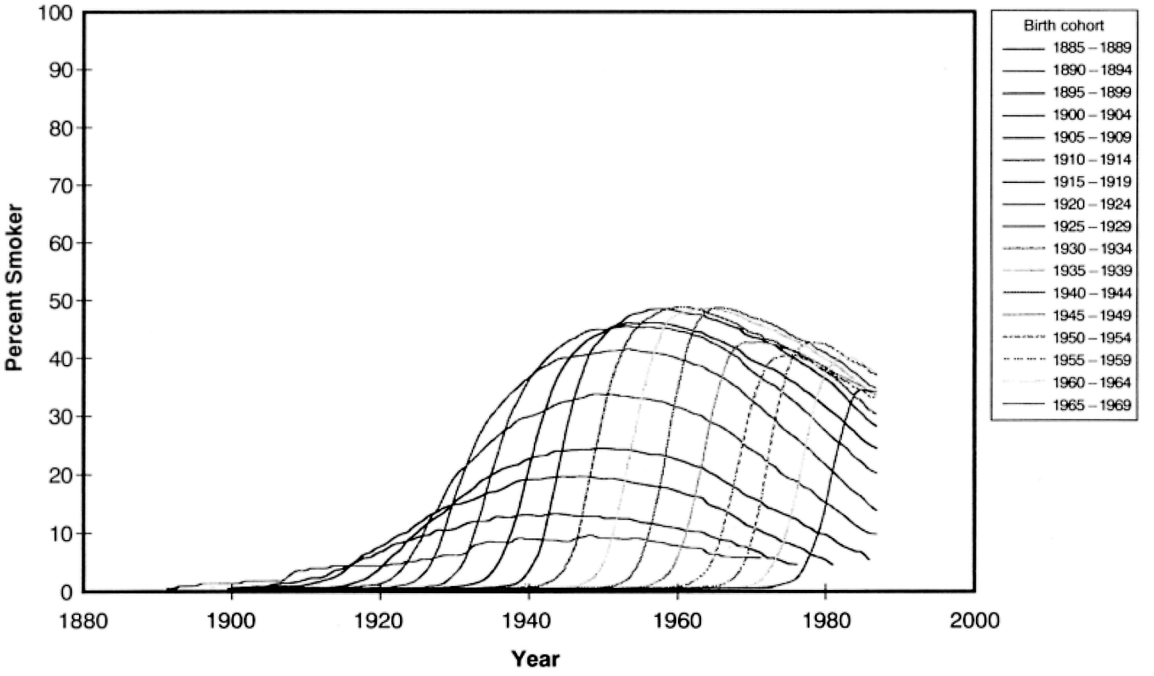
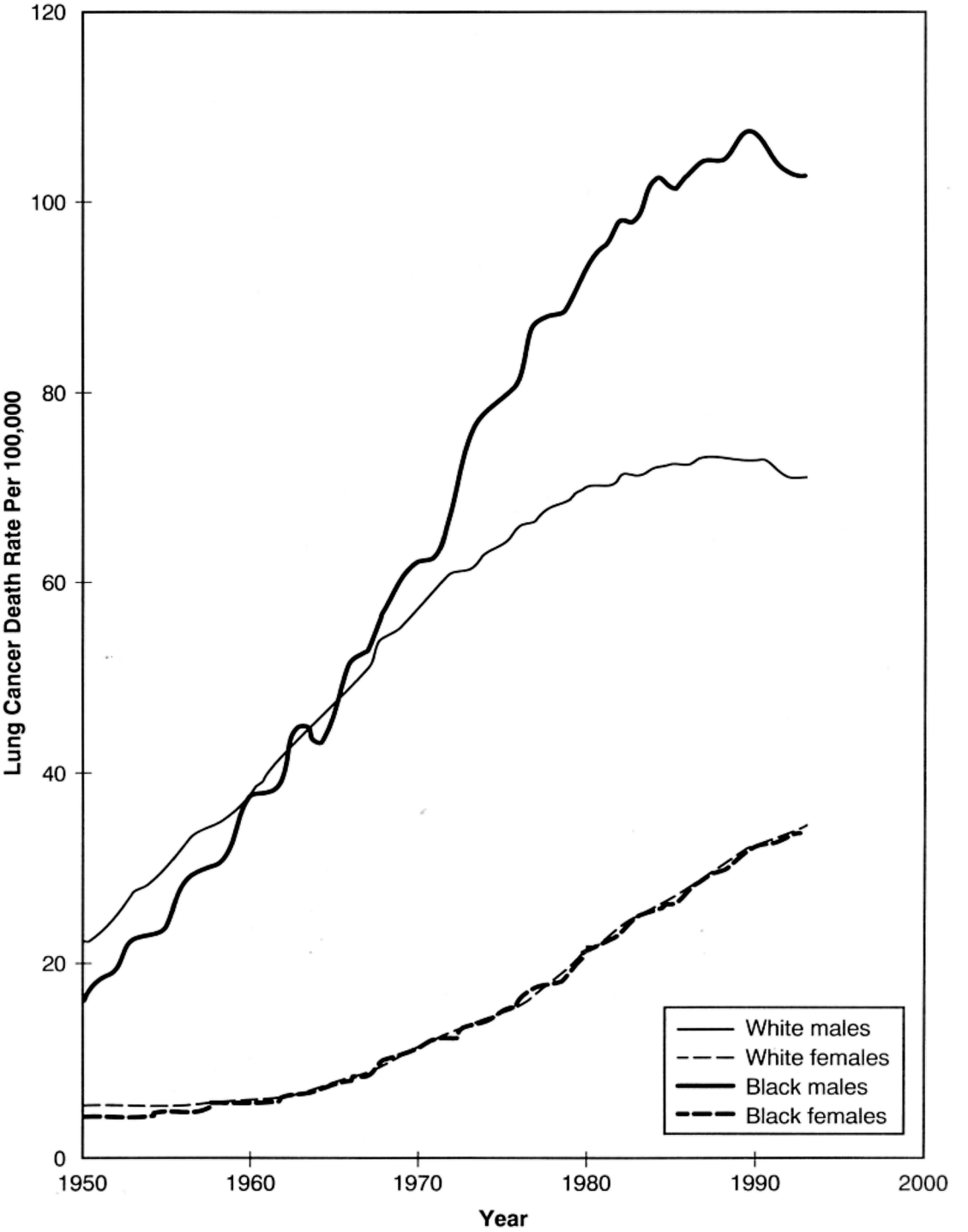


Figure 3
U.S. lung cancer death rates, 1950 to 1993



TRENDS IN SMOKING CESSATION

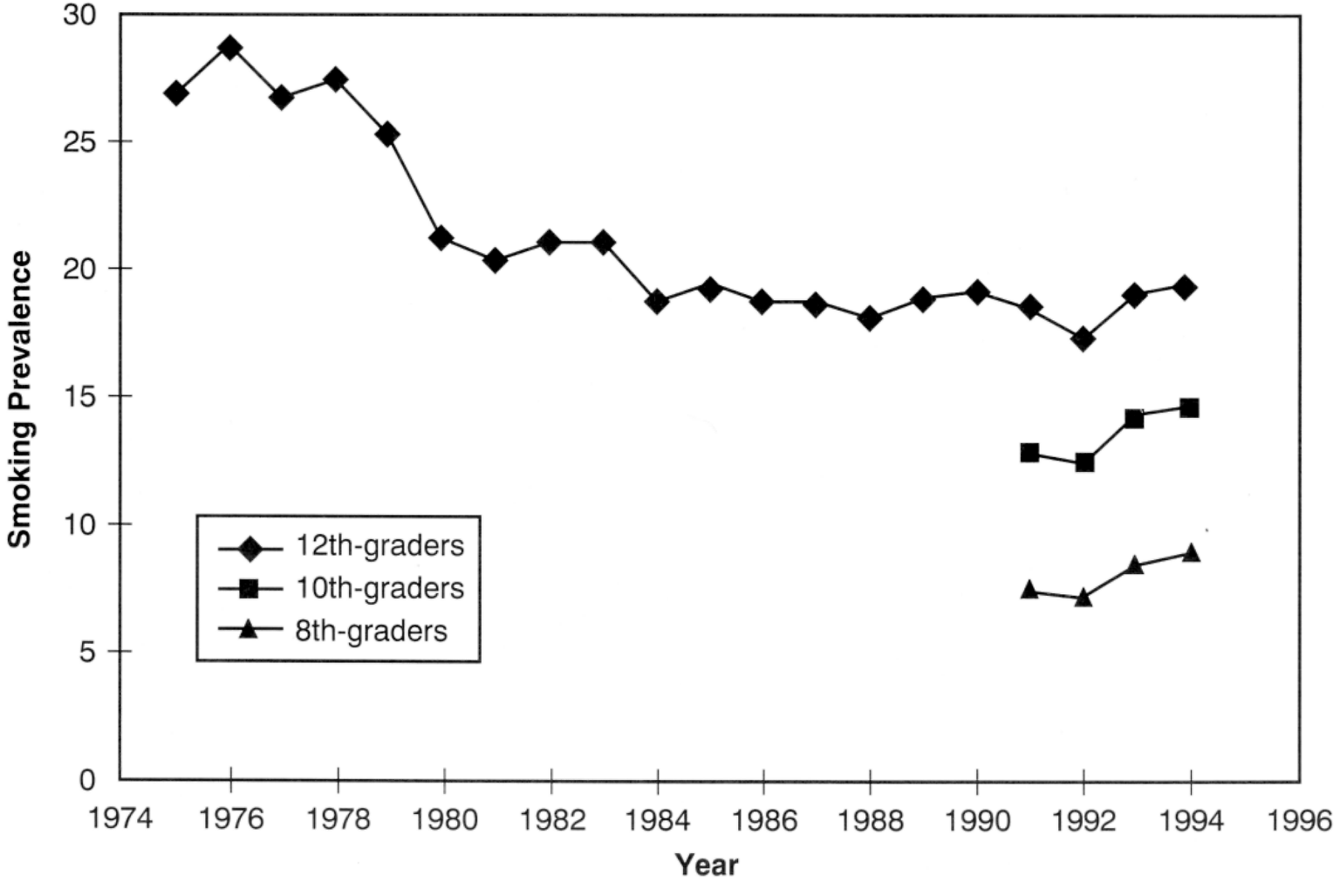
Successful cessation of cigarette smoking was uncommon prior to 1950, probably due to the addictive nature of cigarette smoking and the lack of a widespread understanding that smoking caused disease. White males began to quit smoking during the mid 1950's, when the substantial disease risks associated with smoking were first widely publicized. A large increase in cessation occurred among males and females of both races during the years 1967 to 1970, which coincided with a substantial tobacco control effort by governmental and nongovernmental agencies concerned about public health as well as with a large counter-advertising campaign on television. Cessation rates declined slightly following 1970 and then increased in the late 1970's and early 1980's.

The 20th century has seen dramatic changes in both smoking initiation and smoking cessation, and these changes are responsible for the epidemic of disease among smokers documented in this volume. Changes in smoking behavior, and in male lung cancer incidence, suggest that we have reached the peak of the disease epidemic among males and may expect declining rates of smoking-induced disease in the future. There is some preliminary evidence that the lung cancer rate was decreased between 1990 and 1995 (Cole and Rodu, 1996). The pattern of smoking behavior and the increasing rates of lung cancer among females suggest that the peak rates of disease among females are yet to be reached; ultimately, however, mortality rates among females also should decline, as they have among females younger than age 45 (Ries et.al., 1994). The projected future decline in disease is not inevitable; it is dependent on continued success in achieving cessation and preventing initiation. Recent data on the prevalence of smoking among high school seniors, as well as among 8th- and 10th-graders, are presented in Figure 4; they suggest that rates of smoking initiation may once again be rising. Recent national adult prevalence data (Centers for Disease Control and Prevention, 1996) also suggest that the decline in adult smoking prevalence may have stopped and that smoking may be increasing even among adults. These trends are of enormous public health concern, and they could eliminate any future decreases in disease-specific death rates.

DISEASE CONSEQUENCES OF SMOKING

The disease consequences of smoking are well documented in reports of the Surgeon General (U.S. Department of Health and Human Services, 1989 and 1990) and in a previous NCI monograph (Haenszel, 1966). This volume updates many of these findings and provides a more comprehensive understanding of the relationships among age, number of cigarettes smoked per day, duration of smoking, and duration of cessation in causation of disease. Estimates based on data from CPS-II demonstrate that 52 percent of deaths from all causes among male current smokers are attributable to cigarette smoking. Among female current smokers, 43 percent of deaths from all causes are attributable to smoking. If overall relative risks for all causes of death for current smokers, former smokers, and never-smokers from CPS-II are used to estimate the smoking-attributable fraction for the entire U.S. population older than age 35, the smoking prevalence rates in 1993 would generate smoking-attributable

Figure 4
Prevalence of daily cigarette smoking among 8th-, 10th-, and 12th-grade students, 1975 to 1994



percentages of 35.25 percent for all male deaths and 21.00 percent for all female deaths. This translates into approximately 569,000 excess deaths in 1993, 354,000 among males and 216,000 deaths among females.

These estimates are higher than those calculated using disease-specific relative risks and number of deaths for each cause of death. For example, the American Cancer Society estimates a total of 419,000 each year. They may overestimate the number of deaths because they include both causes of death for which smoking is synergistic with other factors in causing disease and diseases for which the association of smoking and disease is not causal (e.g., cirrhosis of the liver) and because they are based on the age distribution of the living population rather than the deaths. On the other hand, estimates derived from counts of specific causes of death ignore the contribution of smoking to overall poor health status. Poor general health may compromise survival for a broad range of diseases, including those not caused by cigarette smoking, and may limit the treatment options available for the patient. The excess deaths that result from poor health status would be excluded from estimates based only on those diseases caused by smoking. It is also possible that smoking makes small causal contributions to a variety of diseases other than those usually listed as caused by smoking. These small contributions might be difficult to identify in disease-specific epidemiologic analyses but would contribute to the all-cause mortality.

It is likely that the true contribution of smoking to overall mortality lies somewhere between the numbers generated by these two estimation techniques. Clearly, tobacco is a dominant causal factor for a wide variety of diseases and needs to be a principal focus for disease prevention efforts among cigarette smokers.

Excess rates of disease caused by cigarette smoking vary with a smoker's age, the number of cigarettes smoked per day, and the duration of smoking. Early age of initiation results in a longer duration of smoking at any given age. However, there is little evidence from the 12-year followup of CPS-I that early initiation results in an increase in lung cancer risk, independent of its contribution to duration of smoking. The excess risk of specific diseases among smokers also varies with age of the smoker. Among younger smokers, the largest excess disease risk results from coronary heart disease (CHD), with a rapid rise in excess lung cancer death rates developing after the smoker reaches age 55. Excess death rates from chronic obstructive pulmonary disease (COPD) rise even later, increasing dramatically after age 65.

CHANGES IN DISEASE RISK OVER TIME

U.S. death rates for CHD, COPD, and lung cancer have have changed dramatically over the past 40 years and vary substantially between males and females. As was discussed earlier, much of the difference between male and female lung cancer death rates can be explained by differences in smoking behaviors. A similar pattern of male and female death is also observed for COPD. Women began to smoke in large numbers later in the century than men; therefore, they have shorter average durations of smoking at any given age than men. In addition, they tend to smoke fewer cigarettes per day and are more likely to use filtered or

low-tar and -nicotine cigarettes. However, lung cancer rates among white females in CPS-I are lower than those of white males, even when stratified by number of cigarettes smoked per day and duration of smoking. This suggests that factors other than number of cigarettes per day and duration of smoking play a role in the differences between male and female lung cancer death rates. These factors may include differences in pattern of inhalation or type of cigarette smoked as well as other factors.

One of the major changes in cause of death over the past 40 years is the decline in deaths from CHD. Substantial changes in cigarette smoking, diet, and treatment of high blood pressure have occurred during this period, which are likely to be directly related to the decline in CHD deaths. Comparison of the CHD death rates in CPS-I and CPS-II (studies begun more than 20 years apart) reveals that CHD death rates declined between CPS-I and CPS-II among both current smokers and never-smokers. The temporal trend was so large that smokers in CPS-II had lower CHD death rates than lifelong never-smokers in CPS-I. However, the fall in CHD death rates between the two studies was slightly larger in proportionate terms among never-smokers than among current smokers.

Age-adjusted death rates for lung cancer increased dramatically between CPS-I and CPS-II among both male and female smokers. Rates for never-smokers changed little between the two studies. The dramatic changes in birth-cohort-specific smoking behavior among white females over time would be expected to result in these differences between the two studies among females. Careful examination of differences between the smoking behaviors of males in the two studies also suggests that much of the difference between male lung cancer death rates can be explained by differences between the smoking behaviors of males in the two studies. However, when age-, duration-of-smoking-, and cigarettes-per-day-specific strata are compared, lung cancer death rates for male smokers of 20 cigarettes per day who have smoked for more than 40 years are higher in CPS-II than in CPS-I.

These changes over time in the relative risks of death for smokers compared to never-smokers also have been reported for another large prospective mortality study, the British Doctors study. The results of 40 years of followup of these physicians (Doll et al., 1994) reveal that relative risks for all-cause mortality among smokers ages 45 to 64 years compared to never-smokers of the same ages increased threefold when the last 20 years of followup were compared with the first 20 years. A similar twofold increase was found for those ages 65 to 84.

CESSATION One of the principal goals of tobacco control efforts is mitigation of the disease consequences of cigarette smoking through promoting smoking cessation. New data on disease risks following cessation of smoking are presented in this volume, and those data reinforce our existing knowledge (U.S. Department of Health and Human Services, 1990) that smoking cessation dramatically reduces the risk of smoking-related illness in comparison with the risks for the continuing smoker.

Timing of this alteration in risk differs with different disease processes. The relative risk of death from CHD among former smokers in the CPS-I, Kaiser Permanente study, U.S. veterans study, and Nurses' Health Study populations approximates that of never-smokers once the smoker has been tobacco-free for 15 or more years. For shorter periods following cessation, the relative risk of CHD death is elevated but declines as the duration following cessation grows longer. In the U.S. veterans study, a small but statistically significant elevated relative risk (RR = 1.1) persisted among former smokers, even using the longest followup period (26 to 36 years).

The relative risk of death from lung cancer is essentially unchanged for the first 5 years following cessation, probably reflecting the long period between carcinogenic transformation of an individual cell and the death that results due to growth or metastatic spread of the lung cancer. Relative risk declines steadily over the period from 5 to 20 years following cessation. However, in contrast to CHD, the risk of death from lung cancer among former smokers remains elevated above that of never-smokers among the U.S. veterans, Kaiser Permanente, and CPS-I study populations, even 20 or more years following cessation.

Changes in relative risk of death from COPD following cessation mimic those for lung cancer. There is a slow decline in risk among former smokers compared to continuing smokers, but an increased risk persists among former smokers in comparison to never-smokers even 20 or more years following cessation.

PUBLIC HEALTH IMPLICATIONS

Data in this monograph describe the enormous disease burden produced by cigarette smoking. The best way to entirely avoid the disease consequences of smoking is to never start smoking. Prevention of smoking initiation has been a major focus of tobacco control efforts, and these efforts have resulted in a substantial reduction in the proportion of adolescents and young adults who become cigarette smokers. As these younger individuals age, the disease burden produced by tobacco among their cohorts also will fall.

However, the vast majority of tobacco-related diseases occur among older individuals, and large numbers of these older individuals are either current or former smokers. Reduction in disease rates among current smokers is best achieved through cessation, and since the mid-1960's substantial increases in cessation rates among smokers have resulted in more than half of the ever-smokers in the United States becoming former smokers. Translation of this achievement in cessation into reductions in disease-specific death rates is slow but will accelerate as larger numbers of the older population become former smokers of long duration. Early evidence of this effect is reflected in the decline in CHD deaths over the past few decades and the more recent suggestion that white male lung cancer incidence and death rates have leveled off and begun to decline.

However, even if everyone who is currently smoking were to quit and no new smokers were to begin, the data presented in this volume suggest

that a substantial burden of smoking-caused disease would persist for the next several decades because of the residual lung cancer and COPD risks that exist for long-term former smokers. The difference between the current enormous number of deaths caused by smoking and this residual disease burden is a disease prevention goal potentially achievable through comprehensive tobacco control programs.

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