

Recent Trends in Lung Cancer Mortality in the United States

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Background: Previous age–period–cohort analyses of lung cancer incidence and mortality rates in the United States have demonstrated a decrease in risk by birth cohort through 1950, consistent with declining trends in smoking prevalence. This study was conducted to examine recent lung cancer trends, including trends among the cohorts born after 1950. **Methods:** Lung cancer mortality rates from 1970 through 1997 for whites aged 24–83 years and for blacks aged 30–83 years were investigated. Using age–period–cohort analyses with 2-year age and 2-year calendar-period intervals, we examined changes in the slope of the trends in birth-cohort and calendar-period effects. All statistical tests are two-sided. **Results:** There was an unexpected, statistically significant moderation in the rate of decrease of the birth-cohort trend in lung cancer mortality for whites born after 1950, with a corresponding smaller and statistically nonsignificant moderation for blacks. These data are consistent with smoking initiation rates: Rates of both cigarette and marijuana smoking initiation increased for children aged 12–17 years from 1965 through 1977. There was a statistically significant decrease in the slope of the calendar-period trend for lung cancer mortality in 1990 for both whites and blacks that was observed primarily in people 55 years of age and older. **Conclusions and Implications:** The birth-cohort pattern of lung cancer mortality after 1950 appears to reflect the early impact of teenage cigarette smoking on lung cancer risk in people under the age of 45 years, although a contribution from marijuana smoking cannot be ruled out. This result provides additional support for increasing smoking cessation and prevention programs for teenagers. The calendar-period decrease in lung cancer mortality after 1990 may reflect the long-term benefits of reductions in tobacco carcinogens in cigarettes and increases in smoking cessation beginning around 1960. [J Natl Cancer Inst 2001;93:277–83]

It is estimated that 552 200 people will die of cancer in the United States in 2000 and that 28% (156 900) of these deaths will be due to lung cancer (1). Cigarette smoking is the primary risk factor for lung cancer, accounting for about 90% of the cases in men and 70% of the cases in women (2–4). Smoking behavior has been shown to vary by birth cohort (5), and lung cancer rates generally show a pattern of birth-cohort risk consistent with the birth-cohort pattern for smoking prevalence in the United States (6–9). In particular, lung cancer mortality peaked in the 1925–1930 birth cohorts among white males and in the 1935–1940 birth cohorts among white females, and the trends in cigarette smoking correspond well with the trends for lung cancer (7).

For men and women born after these cohorts with peak risk, the birth-cohort risk of lung cancer declined continuously up

until about 1950 (7). The age-adjusted lung cancer mortality rate has declined among males since 1990 (10) and, while the rate among females is still increasing, the rate of increase has diminished considerably (10,11). Thus, overall lung cancer trends are favorable. However, the lung cancer mortality for birth cohorts after 1950 has not been evaluated. Smoking trends in teenagers have not consistently shown the decreases evident in overall smoking trends (12), and the implications of unfavorable smoking trends in teenagers (13) with regard to trends in lung cancer risk are unknown.

We present the results of age–period–cohort analyses of lung cancer mortality data from 1970 through 1997 to evaluate recent lung cancer trends.

SUBJECTS AND METHODS

The mortality rates are calculated from data collected by the National Center for Health Statistics (Hyattsville, MD), which receives death certificates from the states and compiles mortality data by race, sex, age, year, and cause of death. For the current study, only white and black men and women in the United States who were reported to have an underlying cause of death from lung/bronchus cancer during the period from 1970 through 1997 were included. We used the International Classification of Diseases, 9th Revision, to classify codes 162.2–162.9 as lung and bronchus cancer deaths (14).

To adjust for age, period, and cohort effects simultaneously, age–period–cohort models were fitted by Poisson regression to the lung cancer mortality data by use of 2-year age and calendar-period intervals as described previously (15). For whites, there were 30 age intervals (ranging from 24–25 years of age to 82–83 years of age), 14 calendar-period intervals (ranging from 1970–1971 to 1996–1997), and 43 four-year birth-cohort intervals (ranging from 1886–1889 to 1970–1973). Each birth cohort will be identified in the text by the third year in the interval. For example, the 1952 birth cohort will refer to people born from 1950 through 1953, and 75% of people in this cohort will have been born in the middle 2 years, 1951 or 1952. Lung cancer mortality rates for blacks under 30 years of age were unstable because of small numbers of lung cancer deaths. For blacks, therefore, there were 27 age intervals (ranging from 30–31 to 82–83 years of age), 14 calendar periods (ranging from 1970–1971 to 1996–1997), and 40 birth-cohort intervals (ranging from 1886–1889 to 1964–1967).

Changes in the slope of the long-term trend in birth cohort or calendar-period effects were examined by use of identifiable parameters defined as differences between two linear contrasts (16). The coefficients for each linear contrast were selected to be those defining the first-degree polynomial in the appropriate set of orthogonal polynomials (16,17). For each identifiable parameter evaluated in this study, dividing the parameter by the sum of the squared coefficients of each linear contrast provides an estimate of the change in the slope of the birth-cohort or calendar-period trend. Each parameter evaluated was selected after examination of the estimated birth cohort and calendar-period effects, but the same parameter was applied to all four race/sex groups. Consistency of the estimates

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See “Notes” following “References.”

across these groups suggests that the reported findings are not false-positive results. A change in the birth-cohort trend usually indicates changes in an etiologic factor, resulting in increasing or decreasing risk, e.g., changes in the prevalence of smoking. A change in the calendar-period trend can indicate the impact of newly introduced or improved medical interventions, a change in ascertainment or coding of cause of death, or possibly, in the case of lung cancer, increased smoking cessation or a change in composition of cigarettes (6,18). Standard errors of the linear contrasts were adjusted for possible overdispersion when the deviance for the full age-period-cohort model exceeded the number of residual degrees of freedom (19). Two-sided *P* values are reported and are considered to indicate statistical significance when they are less than .05.

RESULTS

Estimates of the birth-cohort effects by race and sex are shown in Fig. 1. The curves show an increase in slope around the year 1950, evidenced by a marked reduction in the rate of decrease of the birth-cohort effects. The slope increase was quan-

tified by use of the identifiable parameter centered on 1950 defined by

$$(5\gamma_{1960} + 3\gamma_{1958} + \gamma_{1956} - \gamma_{1954} - 3\gamma_{1952} - 5\gamma_{1950}) - (5\gamma_{1950} + 3\gamma_{1948} + \gamma_{1946} - \gamma_{1944} - 3\gamma_{1942} - 5\gamma_{1940}),$$

where γ_h denotes the birth cohort effect for the cohort identified by the year *h*. This parameter is the difference between two linear contrasts, the first contrast characterizing the slope of the birth-cohort curve from 1950 through 1960 and the second contrast characterizing the slope from 1940 through 1950. A positive value for this parameter denotes an increase in the birth-cohort slope in 1950, indicating a worsening of the birth-cohort trend in lung cancer mortality after 1950. The magnitude of the increase in slope can be estimated by dividing the parameter by 70. The estimate of the change in cohort slope (per year) is 0.037 (*P* = .0001; 95% confidence interval [CI] = 0.018 to 0.056) for

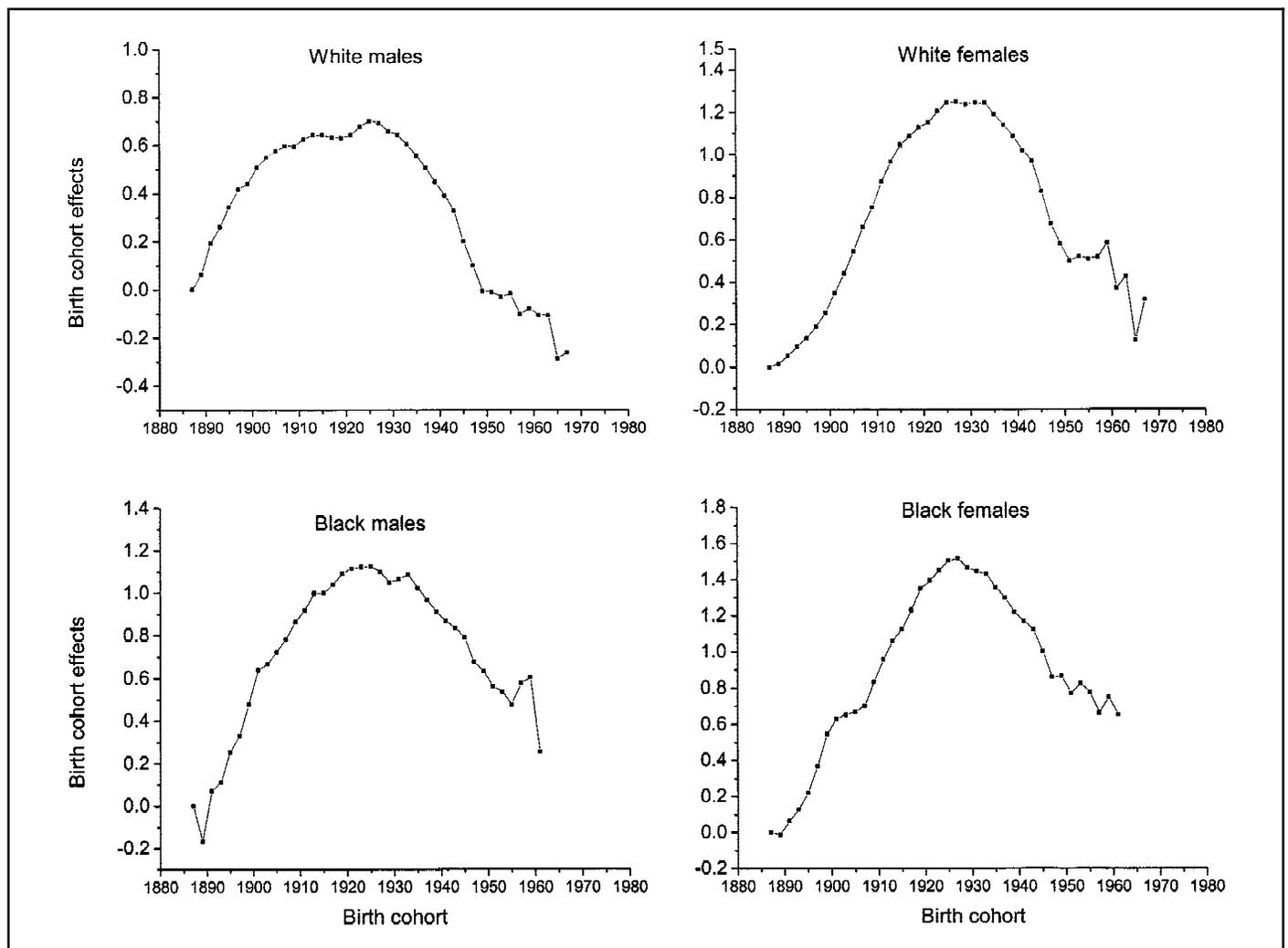


Fig. 1. Maximum likelihood estimates of birth-cohort effects for age-period-cohort analyses of lung cancer mortality data for white and black men and women in the United States. Because of the linear relationship between year of birth, year of death, and age at death (i.e., if any two of these quantities are known, then the third can be calculated), a constraint must be imposed on the model parameters to obtain the estimates. Different estimates will be obtained under different constraints; thus, the individual birth-cohort effects do not necessarily have an interpretation in terms of relative risk. Changes in the slope of the birth-cohort effect curves are, however, independent of the constraint em-

ployed and, thus, can be identified unequivocally, indicating changes in the birth-cohort risk of lung cancer. The estimates were obtained under the constraint that the final birth-cohort effect (i.e., for the 1971 birth cohort for whites and for the 1965 birth cohort for blacks) is zero. The last two birth-cohort effects, including the final constrained birth-cohort effect, are not plotted. Each 4-year birth cohort is identified by the third year (e.g., the 1950 birth cohort refers to people born from 1948 through 1951, with 75% born in 1949 or 1950 and 25% born in 1948 or 1951).

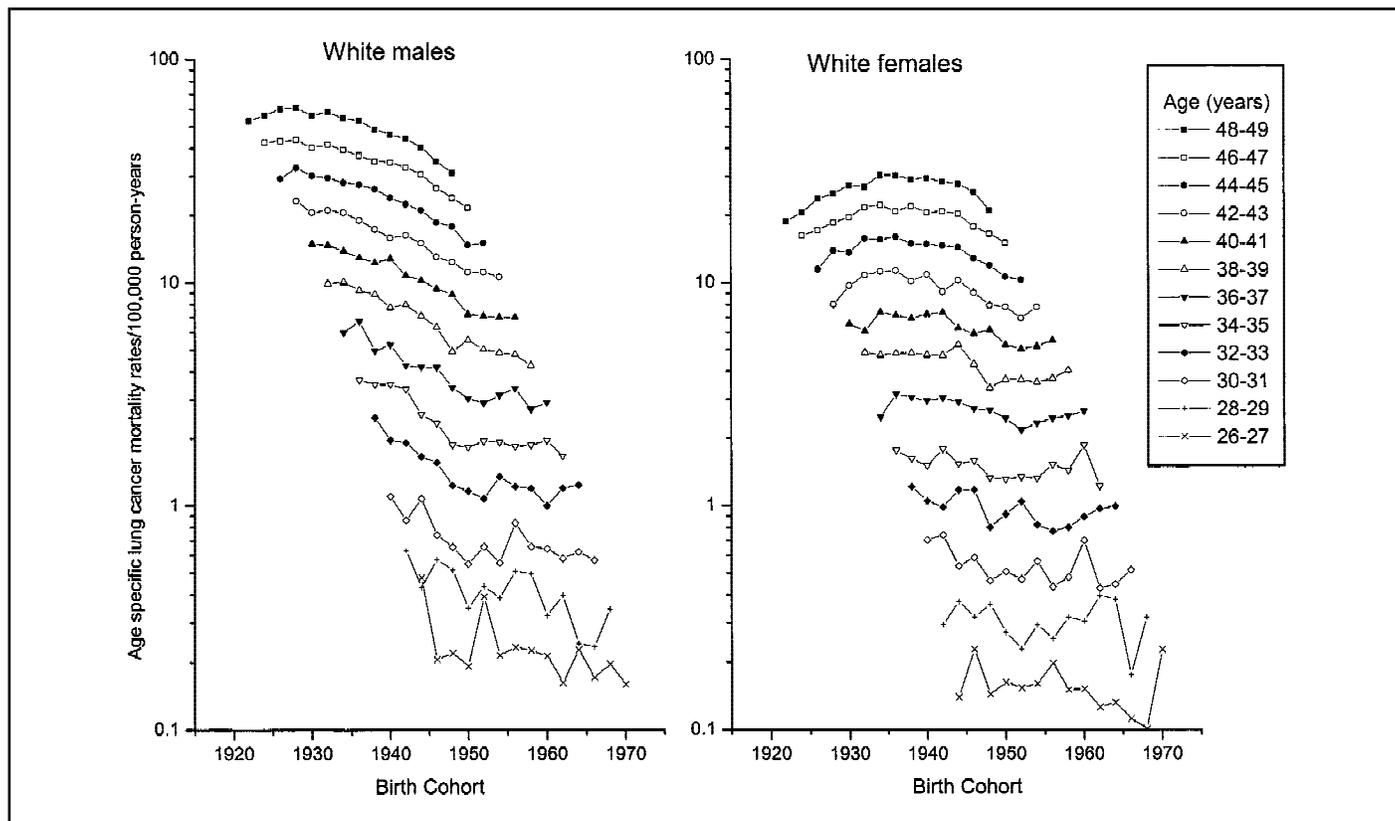


Fig. 2. Age-specific lung cancer mortality rates by 2-year age intervals from 26–27 years of age through 48–49 years of age for white men and women in the United States plotted against birth cohort. Birth cohorts are identified as in Fig. 1.

white males, 0.054 ($P < .0001$; 95% CI = 0.032 to 0.076) for white females, 0.027 ($P = .11$; 95% CI = –0.006 to 0.060) for black males, and 0.027 ($P = .14$; 95% CI = –0.008 to 0.062) for black females. The 2-year age-specific rates for white males and females are plotted by year of birth in Fig. 2. The increased birth-cohort slope in 1950 can be seen in a slowing of the decline in the rates after 1950 in almost all age intervals, demonstrating that the increased birth-cohort slope is not an artifact of the model fitting (e.g., certain interactions, such as increases or decreases in the calendar-period slope with increasing age intervals, can give the appearance of a change in the birth-cohort slope in log-linear modeling). There are indications of a short period of declining birth-cohort risk after 1960 for whites.

Fig. 3 shows rates of smoking initiation for cigarettes and marijuana in children 12–17 years of age (20) as well as the percentage of high school seniors who reported smoking cigarettes daily (21). Teenage smoking trends were similar for males and females. The initiation rates show increases from 1965 to the late 1970s and short-term decreases beginning in the late 1970s. The percentage of high school seniors who smoked daily decreased after 1977, with only a short-term decrease in whites, but the percentage increased around 1992 for both whites and blacks, with a sharper increase in whites.

Estimates of the calendar period effects by race and sex are shown in Fig. 4. Increasing linear trends have been removed (22) from the calendar-period effect curves for females (the calendar-period effects increased 0.024 per year for both white and black females) so that the male and female curves can be plotted on similar scales. Calendar-period mortality decreased sharply around 1990, and the decrease was quantified by use of the

identifiable parameter centered on the 1990–1991 calendar period defined by

$$(3\pi_{1996-1997} + \pi_{1994-1995} - \pi_{1992-1993} - 3\pi_{1990-1991}) - (3\pi_{1990-1991} + \pi_{1988-1989} - \pi_{1986-1987} - 3\pi_{1984-1985}),$$

where the π_j s denote the calendar-period effects. A negative value for this parameter denotes that the slope of the calendar-period risk curve decreased around 1990, indicating an improvement in the calendar-period trend for lung cancer mortality after 1990. The magnitude of the decrease in slope can be estimated by dividing the parameter by 20. The estimates of the change in calendar-period slope (per year) are –0.012 (95% CI = –0.014 to –0.010) for white males, –0.013 (95% CI = –0.016 to –0.010) for white females, –0.021 (95% CI = –0.029 to –0.013) for black males, and –0.019 (95% CI = –0.028 to –0.010) for black females ($P < .0001$ for all four contrasts). Examination of age-specific rates (data not shown) indicates that the calendar-period decrease in slope is apparent primarily in people 55 years of age and older, and age–period–cohort analyses of Surveillance, Epidemiology, and End Results (SEER)¹ incidence rates (data not shown) indicate a similar decrease in calendar-period slope around 1990 for white and black men and women.

DISCUSSION

The moderation in the rate of decrease of the birth-cohort trend in lung cancer risk after 1950 was unexpected on the basis of previous age–period–cohort analyses of U.S. lung cancer

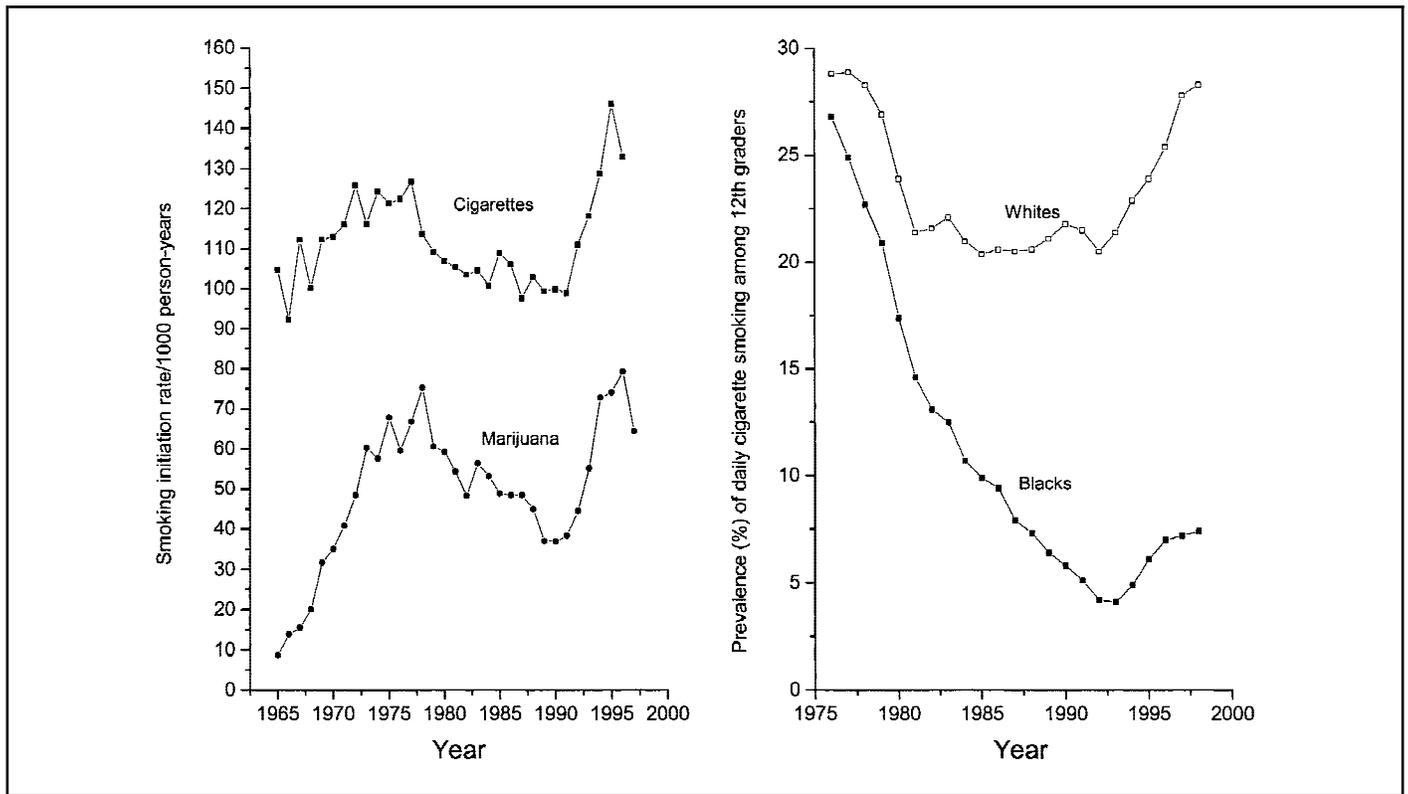


Fig. 3. Cigarette and marijuana smoking rates in teenagers. **Left panel:** rates of initiation of smoking cigarettes and of smoking marijuana between the ages of 12 and 17 years from the National Household Survey on Drug Abuse conducted by the Substance Abuse and Mental Health Services Administration (20). The numerator of the initiation rate is the number of people smoking for the first time

in a given year; all first-time smokers are assumed to have begun smoking in the middle of the year in the calculation of person-years. **Right panel:** daily cigarette smoking prevalence rates for high school seniors in the United States from an annual survey of a nationally representative sample of high school seniors conducted by the University of Michigan Institute for Social Research (21).

rates and on the basis of overall decrease in smoking prevalence in recent decades. The birth-cohort pattern after 1950 is determined by lung cancer trends in people under the age of 45 years and, thus, may reflect the smoking patterns of teenagers and young adults. Indeed, the data showing an increase in smoking initiation from 1965 through 1977 in children 12–17 years of age and a short-term decrease in smoking in white high school seniors after 1977 are consistent with the observed pattern of birth-cohort risk after 1950. Teenage smoking data relevant to the increase in birth-cohort risk around 1950 are incomplete. In particular, it cannot be determined whether the increase in teenage smoking before the late 1970s (Fig. 3) represented a change from the teenage smoking trends before 1965. Nonetheless, the increase in birth-cohort risk of lung cancer mortality around 1950 may reflect a failure of widespread tobacco control efforts by governmental and private health agencies in the 1960s (12) to penetrate the cultural and social factors that influenced smoking onset in children (23–26).

It is possible that marijuana smoking contributed to the birth-cohort pattern of risk after 1950. Marijuana smoke contains many of the same carcinogens found in cigarettes, and marijuana smoke condensate is carcinogenic in experimental animal systems (27,28). Accumulating evidence from studies of histopathologic and molecular changes in lung tissue of smokers suggests that marijuana smoking could increase the risk of lung cancer in humans (29–31), although an epidemiologic study (32) demonstrated no increased lung cancer risk for smoking marijuana, despite a statistically significant increase in lung cancer risk for smoking cigarettes. If marijuana smoking causes lung cancer, it

is possible that increased smoking of marijuana by teenagers and young adults in the 1960s and 1970s contributed to the birth-cohort increase in lung cancer mortality around 1950. Trends in first use of marijuana for ages 12–17 years were quite similar to those for cigarette smoking (Fig. 3). Regardless of the relative contributions of cigarette smoking and marijuana smoking to lung cancer risk, the sharp increase in use of both cigarettes and marijuana since 1991 among teenagers will likely be reflected by an increase in the birth-cohort slope for lung cancer risk for people born around 1975.

Although the peaks of the birth-cohort effect curves for men and women appear to have occurred at approximately the same time (Fig. 1), peaks of birth-cohort effect curves are not identifiable (i.e., the location of a peak is not determined uniquely) in age–period–cohort analyses (see legend to Fig. 1) (16). Age–cohort analyses show that the peak birth-cohort risk occurred in 1923 for men and in 1931 for women (data not shown), consistent with the earlier use of cigarettes by men (5–7,12).

There were no dramatic improvements in lung cancer treatment that could explain the calendar-period decrease in mortality rates around 1990. Five-year relative survival rates from 1974–1976 to 1989–1996 increased in whites, but only from 12.5% to 14.4%, and decreased in blacks from 11.5% to 11.3% [Table XV-7 in (33)]. Moreover, decreases in the slopes of incidence rate curves were observed in white and black men and women around 1990 [Fig. XV-5 in (33)], which suggests that the mortality decrease is a result of a decrease in lung cancer risk, not of an improvement in survival. Although changes in the prevalence of risk factors usually alter the pattern of risk seen

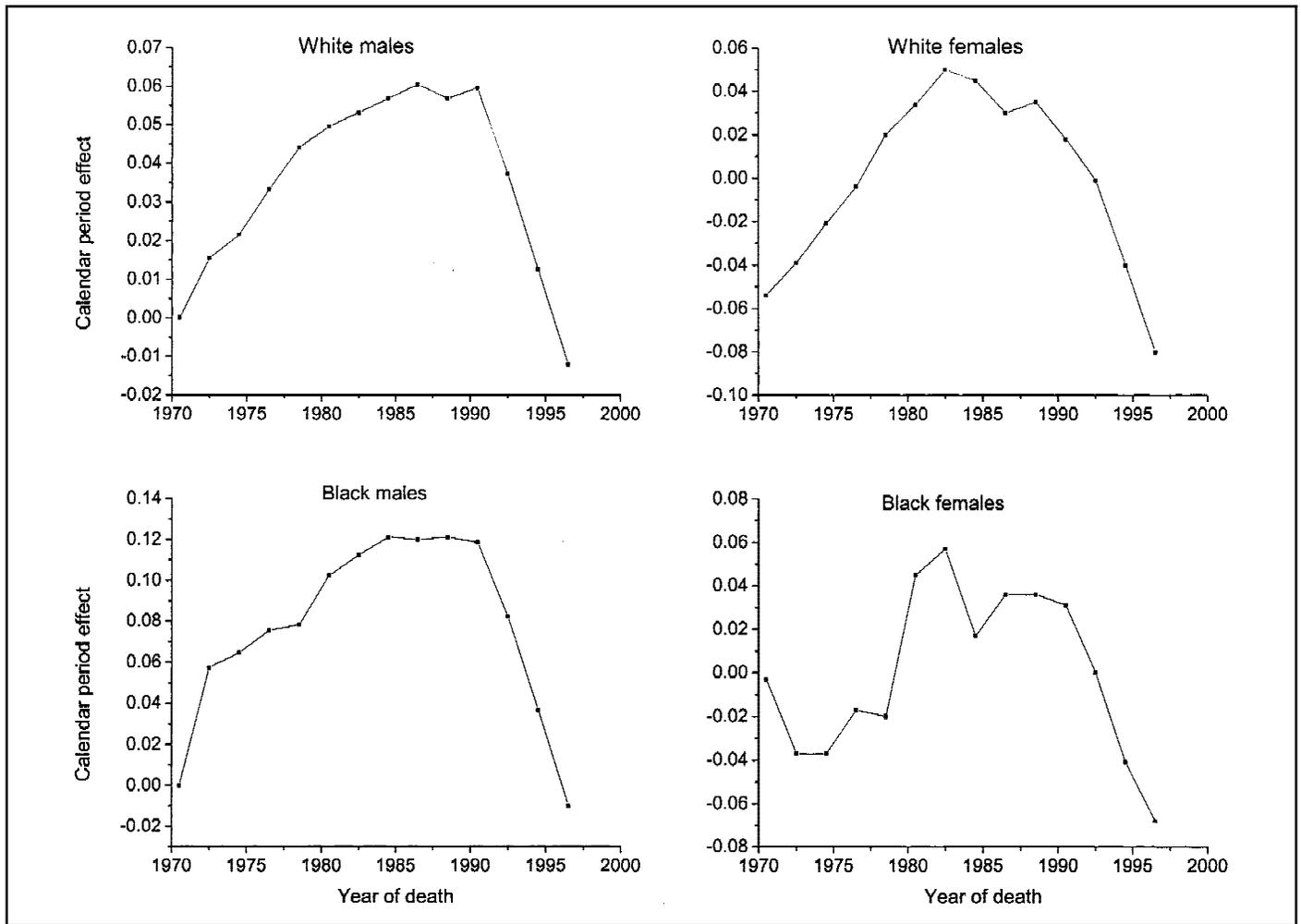


Fig. 4. Maximum likelihood estimates of calendar-period effects for age–period–cohort analyses of lung cancer mortality data for white and black men and women in the United States. Because of the linear relationship between year of birth, year of death, and age at death (i.e., if any two of these quantities are known, then the third can be calculated), a constraint must be imposed on the model parameters to obtain the estimates. Different estimates will be obtained under different constraints; thus, the individual calendar-period effects do not

necessarily have an interpretation in terms of relative risk. Changes in the slope of the calendar-period effect curves are, however, independent of the constraint employed and, thus, can be identified unequivocally, indicating changes in the calendar-period risk of lung cancer. The estimates were obtained under the constraint that the final birth-cohort effect is zero. Each 2-year calendar period is identified by the first year (e.g., 1990 refers to deaths in 1990 or 1991).

among birth cohorts, a substantial decrease in a relatively common carcinogenic exposure could cause a calendar-period decrease in risk after a sufficient latency period. Cigarette smoking affects both early and late stages of the carcinogenic process (34–37). The effect of reducing tobacco carcinogen exposure on the late stage will be seen soon after the change in exposure. Thus, the generally convex shape of the calendar-period effect curves from 1970 through 1990 (Fig. 4) likely reflects the impact of the steadily improving trends in both carcinogen exposure from cigarettes (evidenced by the sharp decline in tar and nicotine yield) and smoking cessation over the study period (Fig. 5) on the late-stage event. In contrast, the effect of reducing tobacco carcinogen exposure on the initiation event will not be observed for decades. The largest decreases in tar and nicotine yield and increases in smoking cessation rates occurred in the 1960s and 1970s. The sharp decline in calendar-period risk around 1990 may reflect the impact on the initiation stage of the decrease in tobacco carcinogen exposure and the increase in smoking cessation beginning around 1960; if so, the impact became manifest only after a latency period of approximately 30

years. The decrease in rates was seen primarily in people old enough (i.e., at least 55 years of age in 1990) to have smoked the high-tar cigarettes for a sufficient duration to show markedly increased lung cancer risk (36). If the 1990 calendar-period decrease reflects the rapid decreases in cigarette carcinogen exposure and increases in smoking cessation between 1960 and 1980, then this calendar-period decrease should continue unabated until at least 2010.

Although caution is warranted in making inferences on the basis of statistical modeling, both the increase in birth-cohort slope in 1950 and the decrease in calendar-period slope in 1990 are evident in plots of age-specific lung cancer rates, indicating that neither change in slope is an artifact of modeling. Age-specific rate curves are remarkably parallel, indicating that there are no major interactions that would complicate interpretation of the age–period–cohort analyses. Speculation about factors causing the changes in lung cancer trends is based on evaluation of population trends in smoking-related factors; as with any such inferences based on grouped data, the possibility of an ecologic fallacy must be considered (40). Cigarette smoking is the pre-

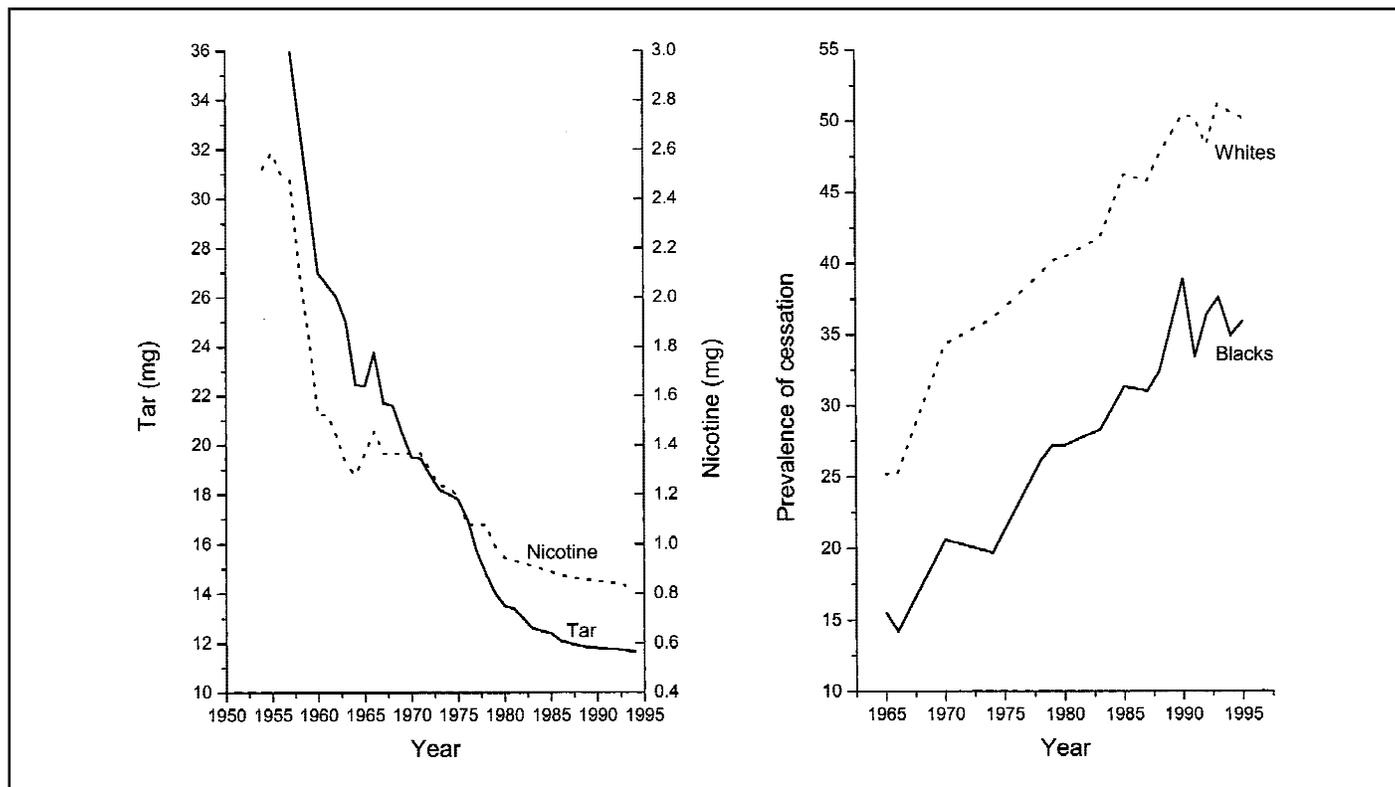


Fig. 5. Left panel: sales-weighted average tar and nicotine yield per cigarette in the United States (38). **Right panel:** percentage of adult (aged 18 years and older) ever cigarette smokers who have quit smoking in the United States from the National Health Interview Studies (39).

dominant cause of lung cancer, however; thus, the changes noted in the lung cancer trend likely have their explanation in changing exposure to cigarette carcinogens. As noted earlier, lung cancer trends over the next decade will provide empiric evidence to either support or contradict the suggested explanations for both slope changes highlighted in this article.

Our study suggests that there may be a rather rapid effect of teenage smoking on lung cancer risk in some people under the age of 45 years and demonstrates that accurate survey data on smoking in children are essential to understanding trends in smoking-related diseases. Thus, continued support should be provided to ongoing national surveys that provide data on teenage smoking. The current trend of teenage smoking is disturbing (13,21,41). Our results suggest that increases in teenage smoking prevalence will lead to increased lung cancer risk for people in their 20s and 30s. This could provide additional incentive to prevent teenage smoking by providing evidence that the harmful effects of smoking occur earlier in life than most teenagers may realize.

REFERENCES

- (1) Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer statistics, 2000. *CA Cancer J Clin* 2000;50:7-33.
- (2) Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. *J Natl Cancer Inst* 1981;66:1191-308.
- (3) U.S. Department of Health and Human Services. Reducing the health consequences of smoking: 25 years of progress. A report of the Surgeon General. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, Center for Chronic Disease Prevention, Office on Smoking and Health. DHHS Publ No. (CDC) 89-8411; 1989.
- (4) Shopland DR. Tobacco use and its contribution to early cancer mortality with a special emphasis on cigarette smoking. *Environ Health Perspect* 1995;103 Suppl 8:131-42.
- (5) Harris JE. Cigarette smoking among successive birth cohorts of men and women in the United States during 1900-80. *J Natl Cancer Inst* 1983;71:473-9.
- (6) Brown CC, Kessler LG. Projections of lung cancer mortality in the United States: 1985-2025. *J Natl Cancer Inst* 1988;80:43-51.
- (7) Devesa SS, Blot WJ, Fraumeni JF Jr. Declining lung cancer rates among young men and women in the United States: a cohort analysis. *J Natl Cancer Inst* 1989;81:1568-71.
- (8) Zheng T, Holford TR, Boyle P, Chen Y, Ward BA, Flannery J, et al. Time trend and the age-period-cohort effect on the incidence of histologic types of lung cancer in Connecticut, 1960-1989. *Cancer* 1994;74:1556-67.
- (9) Cummings KM. Changes in the smoking habits of adults in the United States and recent trends in lung cancer mortality. *Cancer Detect Prev* 1984;7:125-34.
- (10) Wingo PA, Ries LA, Giovino GA, Miller DS, Rosenberg HM, Shopland DR, et al. Annual report to the nation on the status of cancer, 1973-1996, with a special section on lung cancer and tobacco smoking. *J Natl Cancer Inst* 1999;91:675-90.
- (11) Chu KC, Baker SG, Tarone RE. A method for identifying abrupt changes in U.S. cancer mortality trends. *Cancer* 1999;86:157-69.
- (12) Burns DM, Lee L, Shen LZ, Gilpin E, Tolley HD, Vaughn J, et al. Cigarette smoking behavior in the United States. In: *Changes in cigarette-related disease risks and their implication for prevention and control. Smoking and tobacco control monograph No. 8*. Bethesda (MD): U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute; NIH Publ No. 97-4213; 1997.
- (13) Trends in cigarette smoking among high school students—United States, 1991-1999. *MMWR Morb Mortal Wkly Rep* 2000;49:755-8.
- (14) World Health Organization (WHO). *Manual of the international statistical classification of diseases, injuries, and causes of death. Vol 1. 9th revision*. Geneva (Switzerland): WHO; 1977.
- (15) Tarone RE, Chu KC. Implications of birth cohort patterns in interpreting trends in breast cancer rates. *J Natl Cancer Inst* 1992;84:1402-10.

- (16) Tarone RE, Chu KC. Evaluation of birth cohort patterns in population disease rates. *Am J Epidemiol* 1996;143:85–91.
- (17) Snedecor GW, Cochran WG. *Statistical methods*. 7th ed. Ames (IA): The Iowa State University Press; 1980. p. 491.
- (18) Day NE, Charnay B. Time trends, cohort effects, and aging as influence on cancer incidence. In: Magnus K, editor. *Trends in cancer incidence: causes and practical implications*. Washington (DC): Hemisphere; 1982. p. 51–65.
- (19) McCullagh P, Nelder JA. *Generalized linear models*. 2nd ed. New York (NY): Chapman & Hall; 1989. p. 126–8.
- (20) Substance Abuse and Mental Health Services Administration. Summary of findings from the 1998 National Household Survey on Drug Abuse. Rockville (MD): U.S. Department of Health and Human Services, SAMHSA, Office of Applied Studies; DHHS Publ No. SMA 99–3327; 1999. p. 105–11.
- (21) Burns DM, Garfinkel L, Samet JM. Introduction, summary, and conclusions. In: *Changes in cigarette-related disease risks and their implication for prevention and control*. Smoking and tobacco control monograph No. 8. Bethesda (MD): U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute; NIH Publ No. 97–4213; 1997.
- (22) Holford TR. The estimation of age, period and cohort effects for vital rates. *Biometrics* 1983;39:311–24.
- (23) Presson CC, Chassin L, Sherman SJ, Olshavsky R, Bensenberg M, Corty E. Predictors of adolescents' intentions to smoke: age, sex, race, and regional differences. *Int J Addict* 1984;19:503–19.
- (24) Mittelmark MB, Murray DM, Luepker RV, Pechacek TF, Pirie PL, Palonen UE. Predicting experimentation with cigarettes: the childhood antecedents of smoking study (CASS). *Am J Public Health* 1987;77:206–8.
- (25) Allen KF, Moss AJ, Giovino GA, Shopland DR, Pierce JP. Teenage tobacco use: data estimates from the teenage attitudes and practices survey, United States, 1989. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Center for Health Statistics. *Advance Data* No. 224, Feb 1993.
- (26) Peterson AV Jr, Kealey KA, Mann SL, Marek PM, Sarason IG. Hutchinson Smoking Prevention Project: long-term randomized trial in school-based tobacco use prevention—results on smoking. *J Natl Cancer Inst* 2000;92:1979–91.
- (27) Hoffman DL, Brunemann KD, Gori GB, Wynder EL. On the carcinogenicity of marijuana smoke. *Recent Adv Phytochemistry* 1975;9:63–81.
- (28) Cohen S. Adverse effects of marijuana: selected issues. *Ann N Y Acad Sci* 1981;362:119–24.
- (29) Taylor FM 3d. Marijuana use as a potential respiratory tract carcinogen: a retrospective analysis of a community hospital population. *South Med J* 1988;81:1213–6.
- (30) Sherman MP, Aeberhard EE, Wong VZ, Simmons MS, Roth MD, Tashkin DP. Effects of smoking marijuana, tobacco or cocaine alone or in combination on DNA damage in human alveolar macrophages. *Life Sci* 1995;56:2201–7.
- (31) Barsky SH, Roth MD, Kleerup EC, Simmons M, Tashkin DP. Histopathologic and molecular alterations in bronchial epithelium in habitual smokers of marijuana, cocaine, and/or tobacco. *J Natl Cancer Inst* 1998;90:1198–205.
- (32) Sidney S, Quesenberry CP Jr, Friedman GD, Tekawa IS. Marijuana use and cancer incidence (California, United States). *Cancer Causes Control* 1997;8:722–8.
- (33) Ries LA, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, et al., editors. *SEER cancer statistics review, 1973–1997*. Bethesda (MD): National Cancer Institute; 2000.
- (34) Doll R. An epidemiologic perspective of the biology of cancer. *Cancer Res* 1978;38(11 Pt 1):3573–83.
- (35) Doll R, Peto R. Cigarette smoking and bronchial carcinoma: dose and time relationships among regular smokers and life long non-smokers. *J Epidemiol Community Health* 1978;32:303–13.
- (36) Peto R, Doll R. The control of lung cancer. In: Mizell M, Correa P, editors. *Lung cancer: causes and prevention*. Deerfield Beach (FL):Verlag Chemie International; 1984. p. 1–19.
- (37) Brown CC, Chu KC. Use of multistage models to infer stage affected by carcinogenic exposure: example of lung cancer and cigarette smoking. *J Chronic Dis* 1987;40:171S–179S.
- (38) Hoffman D, Djordjevic MV, Brunnemann KD. Changes in cigarette design and composition over time and how they influence yields of smoke constituents. *J Smoking Rel Disorders* 1996;6:9–23.
- (39) Giovino GA, Schooley MW, Zhu BP, Chrismon JH, Tumar SL, Peddicord JP, et al. Surveillance for selected tobacco use-behaviors—United States, 1900–1994. *Mor Mortal Wkly Rep CDC Surveill Summ* 1994;43:1–43.
- (40) Piantadosi S, Byar DP, Green SB. The ecological fallacy. *Am J Epidemiol* 1988;127:893–904.
- (41) Tobacco use among high school students—United States, 1997. *Mor Mortal Wkly Rep CDC Surveill Summ* 1998;47:229–33.

NOTES

¹*Editor's note:* SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

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