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Age-period-cohort analysis of cancers not related to tobacco, screening, or HIV: Sex and race differences

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Abstract

Objective—To identify trends in a residual category of cancers not typically associated with tobacco, screening, or human immunodeficiency virus (HIV) infection.

Methods—For persons aged 20–84 years, we used sex- and race-specific age-period-cohort (APC) models to describe temporal patterns of incidence (1975–2004) and mortality (1970–2004) in the U.S. for a residual cancer category that excluded non-Hodgkin lymphoma, Kaposi sarcoma, and cancer of the oral cavity and pharynx, esophagus, pancreas, larynx, lung and bronchus, urinary bladder, kidney and renal pelvis, colon and rectum, prostate, female breast, and cervix uteri.

Results—Age-specific incidence rose (0.1 – 0.9% per year, on average) in every sex-race group, with factors related to both time period and birth cohort membership appearing to accelerate the increases in women. Age-specific mortality fell (0.6 – 0.9% per year, on average) for black and white men and women, with the declines decelerating in white women but accelerating in the other sex-race groups. Extrapolations of APC models predicted higher age-adjusted incidence rates in white women (11%), black women (5%), and white men (4%) in 2005-09, relative to 2000-04, and lower rates in black men (−3%), accompanied by lower age-adjusted mortality rates in every sex-race group (−8% in black men, −3% in black women, −1% in white men, and −1% in white women).

Conclusions—The possibility that increased incidence in women over time reflects changes in underlying risks, diagnostic practices, or better case ascertainment should be actively explored. Declining mortality may signify improvements in cancer care.

Introduction

After steadily increasing for years, United States (U.S.) age-adjusted all-cause cancer incidence and mortality began falling in the early 1990s.[1] These recent trends, though long awaited, do not apply equally to every population subgroup and cancer type. Understandably, the white population and common cancers (*e.g.* lung, colon, breast, and prostate) dominate overall trends. Counter to the overall trend, for example, age-adjusted incidence increased during the 1995–2004 time period for melanoma of the skin and for cancers of the kidney and renal pelvis, liver and intrahepatic bile duct, and thyroid.[1] Long-term improvements in age-specific cancer mortality (1950–2004) have been observed for deaths that occurred before, but not after, age

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65 years.[2] Likewise, the decline in age-adjusted cancer mortality during the most recent portion of that time period is proportionally greater for deaths before age 65 years.3

Cigarette smoking affects lung cancer trends4 and screening affects colon, breast, and prostate cancer trends.5–7 Also, especially in young adult men, the human immunodeficiency virus (HIV) epidemic has generated a parallel trend in the incidence of non-Hodgkin lymphoma, a relatively common malignancy not typically associated with tobacco or screening.[8] To recognize trends related to changes in cancer risk, including risks mediated by exposures to environmental and occupational carcinogens, or trends related to general improvements in cancer care, it may help to exclude cancers related to smoking, screening, or HIV. Although changes in case ascertainment (including delayed reporting), coding practices, and erroneous population counts can affect trends, scrutiny of trends involving a more narrowly defined cancer category may liberate overall assessments of progress against cancer from the effects of improved tobacco control and early cancer detection.9

Using methods described by Holford[10] and Dinse *et al*.,11 we fitted sex- and race-specific age-period-cohort (APC) models to incidence and mortality rates for cancers not related to tobacco, screening, or HIV. Our category of cancers not related to tobacco, screening, or HIV included 25% of all incident invasive cancer (1975–2004, 9-registry SEER)[12] and 28% of all cancer deaths (1970–2004, U.S.)13. We used results from the APC models to summarize long-term trends and to forecast incidence and mortality into the next 5-year time period.

Methods

Data sources

SEER*Stat (version 6.2.4) provided sex-, race-, age-, and calendar year-specific invasive cancer incidence[12] counts for 1975–2004, cancer mortality13 counts for 1970–2004, and population sizes12, 13 for 1970–2004. Factors to correct incidence counts for reporting delay came from the National Cancer Institute.[14, 15]

The cancer incidence data source covered the populations in the original nine registries participating in the Surveillance, Epidemiology, and End Results (SEER) Program: Connecticut, Hawaii, Iowa, New Mexico, Utah, Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound. Classification according to primary cancer site used the “SEER Incidence Site Recode ICD-O-3, 1/27/2003” (http://seer.cancer.gov/siterecode), a coding scheme that maps ICD-O-3 primary site and histology data (converted from ICD-O-2, where necessary) into conventional temporally consistent primary site groupings. The cancer mortality data source covered the entire U.S., including all 50 states and the District of Columbia. Classification according to cause of 5 death used the “SEER Cause of Death (COD) Recode 1969+, 9/17/2004” (http://seer.cancer.gov/codrecode), a scheme that maps ICD-9 (converted from ICD-8, where necessary) and ICD-10 cause of death codes into conventional temporally consistent cause of death groupings. The category of cancers not related to tobacco, screening, or HIV excluded non-Hodgkin lymphoma, Kaposi sarcoma (incidence) or other non-epithelial skin cancer (the Kaposi sarcoma-equivalent mortality category), and cancer of the oral cavity and pharynx, esophagus, pancreas, larynx, lung and bronchus, urinary bladder, kidney and renal pelvis, colon and rectum, prostate, breast (women), and cervix uteri. To enable comparison, analyses applied the definitions used by Dinse *et al*.[11] to specify cancers related to tobacco or screening.

Statistical analysis

Separately for each sex-race group (white men, black men, white women, and black women), we plotted logarithmically scaled age-specific rates (in 5-year age groupings from 20–24

through 80–84 years) as a function of calendar time (in 5-year intervals from 1975-79 through 2000-04 for incidence (corrected for reporting delay) and from 1970-74 through 2000-04 for mortality). We chose not to model cancer endpoints occurring after age 84 years, a setting where variability in medical care affects the recognition and classification of cancer.

For each sex-race group, we used Poisson regression (PROC GENMOD in SAS, Version 9.1, Cary, NC) to fit APC models that expressed the logarithms of cancer incidence and mortality rates as functions of age group, time period, and birth cohort (see Appendix). If residuals under the fitted APC model were over-dispersed ($p<0.05$; Pearson goodness-of-fit test), we accommodated extra-Poisson variation with a procedure developed by Breslow.[16] Based on methods described by Holford10 and Dinse *et al*.,[11] the effects of each temporal factor were characterized by a slope that quantifies long-term linear trend and a collection of deviations from that trend line. Placing no constraints on the age parameters, we considered three models for incorporating time effects due to period and cohort: (i) the full APC model, which places no constraints on the period or cohort parameters, (ii) the constant-curvature model, which constrains the period and cohort effects to be quadratic functions of time, and (iii) the linear time trend model, which constrains the period and cohort effects to be linear functions of time.

The full APC model includes a slope and a collection of deviations for each temporal factor (Appendix).[10, 11] The linear time trend model retains all three slopes and the age deviations, but eliminates the period and cohort deviations. The constant-curvature model expands the linear time trend model by adding the squares of the linear period and cohort terms.

We plotted period and cohort deviations to identify time-related patterns of change and to informally evaluate the appropriateness of the constant-curvature model relative to the full APC model. We used likelihood ratio tests to formally compare APC models and to evaluate the statistical significance of certain parameters. We estimated age-specific risks in 2005-09 by incrementing the period and cohort terms in the constant-curvature model by one five-year time unit.

Under the full APC model, we calculated the average annual percent change (AAPC) in age-specific incidence between 1975 and 2004 and in age-specific mortality between 1970 and 2004. The AAPC provides an estimate of the long-term linear trend in logarithmically scaled cancer rates over time, though distinct period and cohort contributions to this linear time trend cannot be identified (Appendix). In contrast, any deviations from linearity (*e.g.*, curvature) can be separated into distinct period and cohort components. As a summary of how age-specific cancer patterns diverge from the constant rate-of-change scenario (*i.e.*, the straight-line time trend on the log scale), we derived the constant curvature index (CCI), which is the product of a time period component (CCI^p) and a birth cohort component (CCI^c) (Appendix). The CCI is the ratio of rate ratios for any adjacent pairs of five-year time intervals under the constant-curvature model, and it indicates the direction and magnitude of the combined period and cohort curvature. Within any age group, the CCI is the expected risk in one time period relative to the previous period, divided by the expected risk in the previous time period relative to the period before that. The CCI is greater (or less) than 1.0 according to whether time plots of logarithmically-scaled age-specific cancer rates curve upward (or downward) over time; that is, whether temporal changes are accelerating (or decelerating).

We based most of our inferences on the AAPC (estimated under the full APC model) and the CCI (estimated under the constant-curvature model). We observed that the AAPC and CCI effectively and efficiently summarized major temporal patterns in incidence and mortality rates. Although the full APC model generally fitted better than the constant-curvature model, the constant-curvature model facilitated extrapolations into future years. We viewed systematic departures of the constant-curvature model from the full APC model as an opportunity to

identify unique influences from specific time periods or specific birth cohorts. A web supplement describes procedures used to compare the constant-curvature and full APC models and to identify time period- or birth cohort-specific effects.

Results

Presenting incidence and mortality separately, the following paragraphs refer, in sequence, to sex- and race-specific age adjusted trends (Figure 1), sex-, race-, and age-specific trends (Figure 2), primary results from APC models (Table), departures of the constant-curvature model from the full APC model (Figure 3), and risk projections from the constant-curvature APC model (Figure 1).

Incidence models

Uncorrected for reporting delay, ten cancer subcategories accounted for 82.4% of cancer incidence not related to tobacco, screening, or HIV in 20–84 year-old white or black men during the 1975–2004 time frame. These subcategories are: melanoma of skin (17.2%), leukemia (13.3%), miscellaneous cancer (11.0%), stomach (10.5%), brain and other nervous system (7.1%), testis (5.9%), myeloma (5.8%), liver and intrahepatic bile duct (4.8%), Hodgkin lymphoma (3.4%), and thyroid (3.4%). Similarly, the following ten cancer subcategories accounted for 84.2% of incidence in women: corpus uteri (22.8%), ovary (12.8%), melanoma of skin (11.0%), miscellaneous cancer (8.3%), leukemia (7.3%), thyroid (7.2%), stomach (4.5%), brain and other nervous system (4.3%), myeloma (3.9%), and Hodgkin lymphoma (2.1%).

In 2000-04, the age-adjusted incidence of invasive cancers not related to tobacco, screening, or HIV was higher in white (178 per 100,000) than black women (140 per 100,000) and higher in white (162 per 100,000) than black men (137 per 100,000; Figure 1). Age-adjusted incidence increased between 1975-79 and 2000-04, a 25-year time span, by 23% in white men, 11% in white women, and 9% in black women. In women, the increase in age-adjusted incidence started in 1985-89. Regardless of sex or race, the long-term trend in incidence appeared to be stable or on the rise in every 5-year age group, except possibly for black men over 60 years old (Figure 2).

Full APC models estimated the increasing incidence trends (AAPC) at 0.88% per year in white men, 0.12% per year in black men, 0.69% per year in white women, and 0.52% per year in black women (Table), statistically significant in each sex-race group except black men (Test 1, Table). Constant-curvature APC models suggested non-linear time trends that curved upward in women (CCI: 1.023 in white women, 1.010 in black women) and downward in men (CCI: 0.997 in white men, 0.990 in black men). Improvements due to fitting constant-curvature rather than linear time trend models (Test 2, Table) were statistically significant. For blacks, the full and constant-curvature APC models were statistically equivalent (Test 3, Table). In white women, the cohort deviation plot (Figure 3) showed that deviations estimated under the constant-curvature model did not closely track deviations estimated under the full APC model, particularly near the fifth (1910-19) through seventh (1920-29) birth cohorts and again near the tenth (1935–1944). These discrepancies corresponded to the full APC model ameliorating the tendency of the constant-curvature model to underestimate risks in the fifth through seventh birth cohorts and to overestimate risks in the tenth. For example, underestimation in the fifth birth cohort can best be seen (Figure 2) for incidence in 55–59 year-old (1915-24 birth cohort) white women during the first time period (1975-79) and in 70–74 year-old (1915-24 birth cohort) white women in the fourth time period (1990-94).

For white and black women, both period and cohort deviations generally appeared to curve upward (Figure 3). Given the long-term incidence upsurge in women (AAPC 0.69% per year

in white women and 0.52% per year in black women; Table), upward curvatures in both the period and cohort deviations imply that factors related to both period and cohort worked together to accelerate increases in age-specific incidence over time.

In 2005-09 relative to 2000-04, constant-curvature APC models predicted increased age-adjusted incidence in white men (4%), white women (11%), and black women (5%) and decreased incidence in black men (−3%) (Figure 1).

Mortality models

Ten cancer subcategories accounted for 90.9% of cancer mortality not related to tobacco, screening, or HIV in 20–84 year-old white or black men during the 1970–2004 time frame. These subcategories are: miscellaneous malignant cancer (27.3%), leukemia (15.0%), stomach (13.1%), brain and other nervous system (9.6%), liver and intrahepatic bile duct (8.2%), myeloma (6.7%), melanoma of skin (5.9%), soft tissue including heart (2.3%), Hodgkin lymphoma (1.9%), and gallbladder (0.9%). Similarly, the following ten cancer subcategories accounted for 88.6% of mortality in women: miscellaneous malignant cancer (21.8%), ovary (18.1%), leukemia (10.2%), corpus uteri (8.7%), stomach (7.3%), brain and other nervous system (7.0%), myeloma (5.6%), liver and intrahepatic bile duct (4.4%), melanoma of skin (3.3%), and gallbladder (2.2%).

In 2000-04, the age-adjusted mortality from cancers not related to tobacco, screening, or HIV was higher in black (93 per 100,000) than white men (75 per 100,000) and higher in black (73 per 100,000) than white women (62 per 100,000; Figure 1). Age-adjusted mortality decreased between 1975-79 and 2000-04, a 25-year time span, in every sex-race group: by 3% in white men, 11% in black men, 10% in white women, and 10% in black women. In men, the decrease in age-adjusted mortality started in 1985-89. Regardless of sex or race, the long-term mortality trend appeared to be stable or falling in nearly every 5-year age group (Figure 2).

Full APC models estimated the decreasing mortality trends (AAPC) at −0.74% per year in white men, −0.62% per year in black men, −0.90% per year in white women, and −0.82% per year in black women (Table), statistically significant in each sex-race group (Test 1, Table). Constant-curvature APC models suggested non-linear time trends that curved upward in white women (CCI: 1.002) and downward in other sex-race groups (CCI: 0.995 in white men, 0.979 in black men, and 0.994 in black women). Improvements due to fitting constant-curvature rather than linear time trend models were statistically significant (Test 2, Table) in each sex-race group. With respect to model fit, full APC models were superior to constant-curvature models (Test 3, Table). Every sex-race group exhibited birth cohort effects on mortality as evidenced by a divergence of age-specific mortality curves through calendar time. Mortality increased, if at all, only in the oldest age groups, and, otherwise, it decreased; and it did so at a relatively more rapid pace in younger age groups (Figure 2). This diverging pattern was broken to some extent in the youngest women, particularly black women. Specifically, we observed that the constant-curvature model underestimated risk in the youngest (most recent) birth cohorts, represented by 20–24 through 30–34 year-old women in the three most recent time periods (1990-94 through 2000-04). This limitation of the constant-curvature model accounted for some of the differences between the full and constant-curvature APC mortality models with respect to the birth cohort deviations estimated for white and black women (Figure 3).

For black men, both period and cohort deviations appeared to curve downward. Given the long-term mortality decline in black men (AAPC −0.62% per year), downward curvatures in both the period and cohort deviations imply that factors related to both period and cohort worked together to accelerate decreases in age-specific mortality over time.

In 2005-09 relative to 2000-04, constant-curvature APC models predicted larger decreases in age-adjusted mortality for blacks (−8% in black men and −3% in black women) than whites (−1% in white men and −1% in white women; Figure 1).

Discussion

We plotted sex- and race-specific time trends for cancers not related to tobacco, screening, or HIV (Figure 1) and, after age-adjusting to the U.S. 2000 standard population, we observed 1) higher incidence in whites than blacks, 2) higher mortality in blacks than whites, 3) higher incidence in 2000-04 than 25 years earlier in 1975-79 (by 23% in white men, 11% in white women, and 9% in black women), and 4) lower mortality in 2000-04 than 25 years earlier in 1975-79 (by 3% in white men, 11% in black men, 10% in white women, and 10% in black women). Beginning in the 1985-89 calendar period, age-adjusted incidence rates decreased in black men but increased in the remaining sex-race groups; age-adjusted mortality decreased in every sex-race group during the same calendar period. To understand how distinct age groups influenced these age-adjusted trends, we used APC models to illuminate patterns in plots of the age-specific rates over time (Figure 2).

The black population in the U.S. is about one-eighth the size of the white population. Moreover, the SEER population (used to calculate cancer incidence) is about one-eleventh the size of the U.S. population (used to calculate cancer mortality). These differences in population sizes contributed to the greater variability and irregularity observed for incidence (relative to mortality) and for blacks (relative to whites) (Figure 2). These differences in population sizes complicated the direct visual interpretation of time plots of age-specific rates and provided further justification for use of APC models.

APC models recognized a statistically significant long-term trend of increasing incidence between 1975 and 2004 in every sex-race group (AAPC: 0.88% per year in white men, 0.69% per year in white women, and 0.52% per year in black women; Table) except black men (AAPC: 0.12% per year). In addition, in women only, time plots of the logarithmically scaled rates tended to curve with calendar time in an upward direction (CCI: 1.023 in white women, 1.010 in black women; Table), a pattern resulting in age-specific incidence increasing with accelerating pace over recent time periods (Figure 2). In plots of expected age-specific incidence (constant-curvature models; Figure 2), recent percentage increases in incidence were clearly seen to be larger in younger than older women. If part of this experience of contemporary younger women is a fixed property of birth cohort membership, where some component of elevated risk tracks with aging into future time periods, then we would predict a future widening in the incidence disparity between women and men (Figure 1).

APC models also recognized a statistically significant long-term trend of decreasing mortality between 1970 and 2004 in every sex-race group (AAPC: −0.74% per year in white men, −0.62% per year in black men, −0.90% per year in white women, and −0.82% per year in black women; Table). In addition, most prominently in black men (CCI: 0.979; Table), time plots of the logarithmically scaled rates tended to curve with calendar time in a downward direction, a pattern resulting in age-specific mortality decreasing with accelerating pace over recent time periods (Figure 2). In plots of expected age-specific mortality (constant-curvature models, Figure 2), recent percentage decreases in mortality were clearly seen to be larger in younger than older black men. If part of this experience of contemporary younger black men is a fixed property of birth cohort membership, where some component of lower mortality tracks with aging into future time periods, then we would predict future narrowing in the large mortality disparity between black and white men (Figure 1).

The full APC model often fitted the data better than the more restrictive constant-curvature model (Test 3, Table). In these instances, we used deviation plots (Figure 3) to identify systematic differences between the full APC and constant-curvature models. For example, one discrepancy between the two incidence models for white women was centered between the fifth (1910-19) and seventh (1920-29) birth cohorts (birth cohorts coming to adulthood during the Great Depression and World War II). In this case, the full APC model worked to correct the tendency of the constant-curvature APC model to underestimate risks in those birth cohorts (Figure 2). For white and black women, the general pattern of contemporary mortality decreasing more rapidly with younger age was attenuated or reversed in the youngest age groups (Figure 2). Continuation of this undesirable attenuation into future birth cohorts of women could reverse the currently observed decline in age-adjusted mortality (Figure 1).

The larger percentage increases in incidence seen in contemporary younger relative to older women invite speculation regarding potential effects from time-related male-female differences in workforce participation,[17] occupational cancer risks,[18] or use of possibly unsafe household cleaning and personal care products.[19]

We extrapolated our constant-curvature models forward in time to forecast incidence and mortality in 2005-09 (Figure 1). The validity of this approach depends on the extent to which our constant-curvature models accurately captured prevailing trends, particularly over recent time periods and birth cohorts. These models predicted higher age-adjusted incidence in every sex-race group, except black men, and lower age-adjusted mortality in every sex-race group.

Notions based on the study of a residual cancer grouping (*i.e.*, cancers not related to tobacco, screening, or HIV) may depend on the choice of cancer sites included in the definition. We also analyzed a residual cancer grouping (cancers not related to tobacco or screening) that included non-Hodgkin lymphoma and Kaposi sarcoma. APC analysis of a residual cancer category that included non-Hodgkin lymphoma and Kaposi sarcoma produced different estimates of long-term trends (AAPC incidence: 1.17% per year in white men, 0.94% per year in black men, 0.82% per year in white women, and 0.83% per year in black women; AAPC mortality: −0.58% per year in white men, −0.43% per year in black men, −0.81% per year in white women, and −0.67% per year in black women). Directions of change were unaltered, though incidence trends increased more rapidly and mortality trends decreased less rapidly. AAPC was statistically significant in incidence models that included non-Hodgkin lymphoma and Kaposi sarcoma (data not shown) and, except for black men, in incidence models that excluded non-Hodgkin lymphoma and Kaposi sarcoma (Table). However, including non-Hodgkin lymphoma and Kaposi sarcoma in the residual cancer grouping adversely affected the fit of even the full APC models. Problems of fit for men occurred because of time trends unique to young adult males that paralleled the U.S. HIV epidemic. To avoid concerns created by poorly fitted models, we excluded non-Hodgkin lymphoma and Kaposi sarcoma from our residual cancer category, conceived our residual cancer category in terms of cancers not related to tobacco, screening, or HIV, and kept the topic of non-Hodgkin lymphoma time trends for a separate manuscript.

Our residual cancer category included two cancers (stomach cancer and acute myeloid leukemia) causally related to smoking20, 21 and two cancers (Hodgkin lymphoma and anal cancer) related to HIV.22 For consistency with our 1999 report,11 we chose to retain stomach cancer, acute myeloid leukemia, Hodgkin lymphoma, and anal cancer in primary analyses. To improve model fit, we excluded NHL and Kaposi sarcoma. Retaining NHL and Kaposi sarcoma, results summarized in the previous paragraph replicated the definitions we used in 1999.

In conclusion, the incidence of cancers not related to tobacco, screening, or HIV is increasing, a result that signifies increasing cancer risks, changing diagnostic practices, or better case ascertainment. Our residual cancer category is necessarily diverse, including cancers increasing and decreasing in frequency. For example, entities contributing to increasing incidence included melanoma of skin, liver and intrahepatic bile duct cancer, and thyroid cancer.[23] Entities counteracting increasing incidence included ovary cancer, stomach cancer, brain and central nervous system cancer, and myeloma.[23] Factors plausibly related to increasing cancer risk include changes in personal behaviors, such as alcohol use, diet, sun exposure, hepatitis B immunization, and sexual practices. Mortality is decreasing, a result that signifies changes in coding practices or, in the setting of increasing incidence, improvements in cancer care. In addition to AAPC estimates of global trends, APC models underscored public health relevant age-specific trends, namely, incidence increasing more rapidly in younger women and mortality decreasing more rapidly in younger black men. Insights into these global and age-specific trends may emerge from future studies, perhaps using APC models, of the distinct cancers in our residual category.

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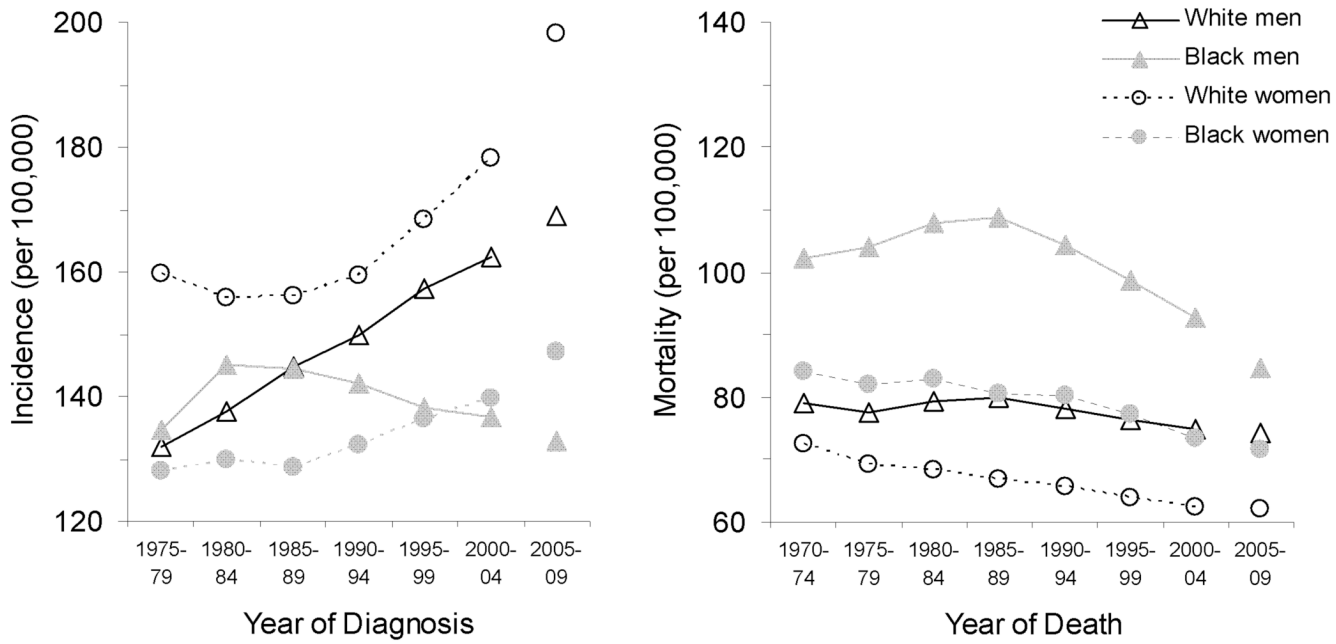

Figure 1.

Age-adjusted (U.S. 2000 standard population) cancer incidence (corrected for reporting delay) and mortality not related to tobacco, screening, or HIV, by sex and race for 20–84 year-old persons. Values shown for the 2005-09 time period are projections based on constant-curvature APC models.

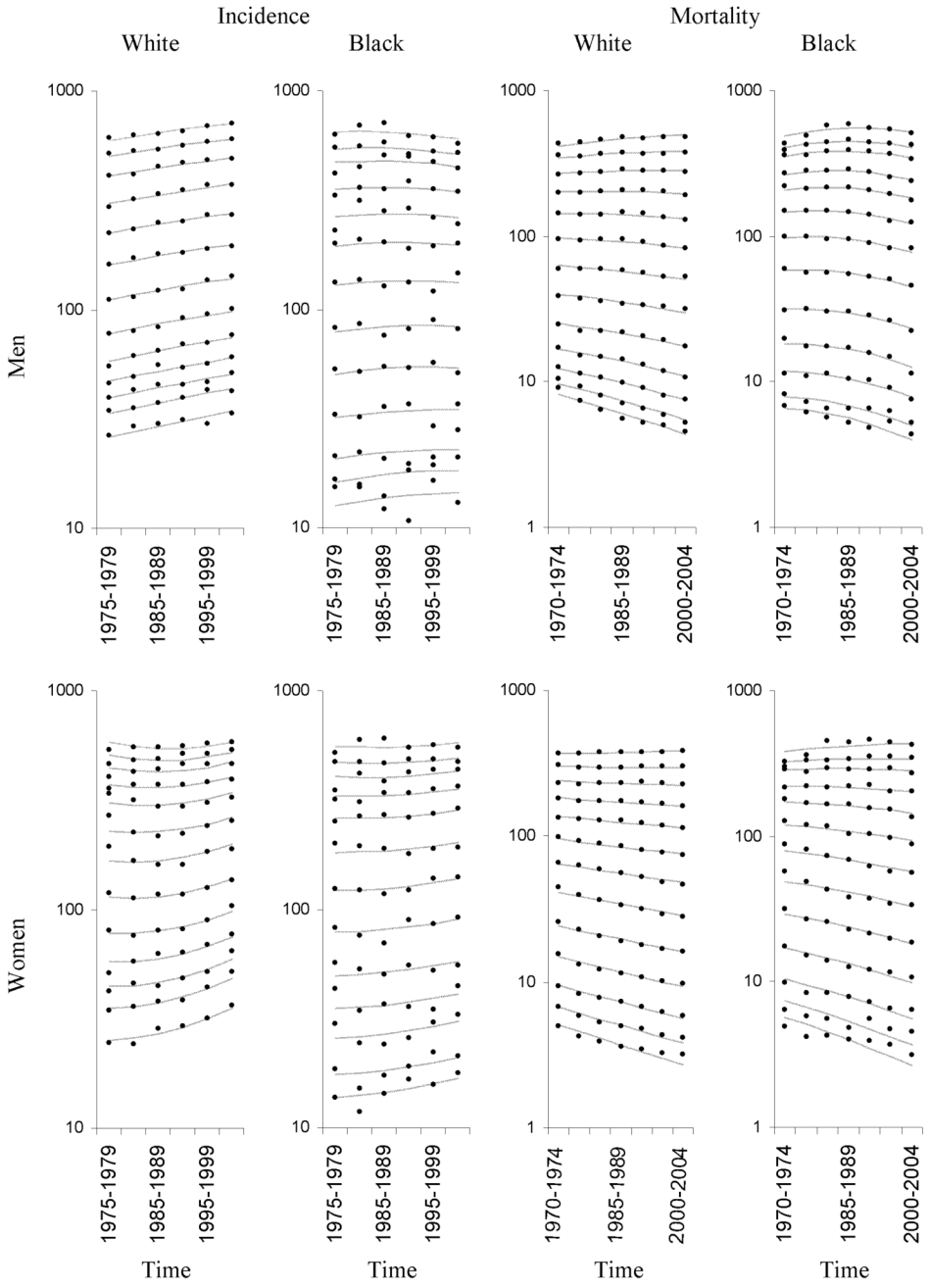

Figure 2.

Time courses of logarithmically scaled incidence (corrected for reporting delay) and mortality for cancers not related to tobacco, screening, or HIV, by sex, race, and age. The continuous curves represent the fit achieved by constant-curvature APC models for increasing 5-year age groupings that start at 20–24 years (lowest curve) and end at 80–84 years (highest curve).

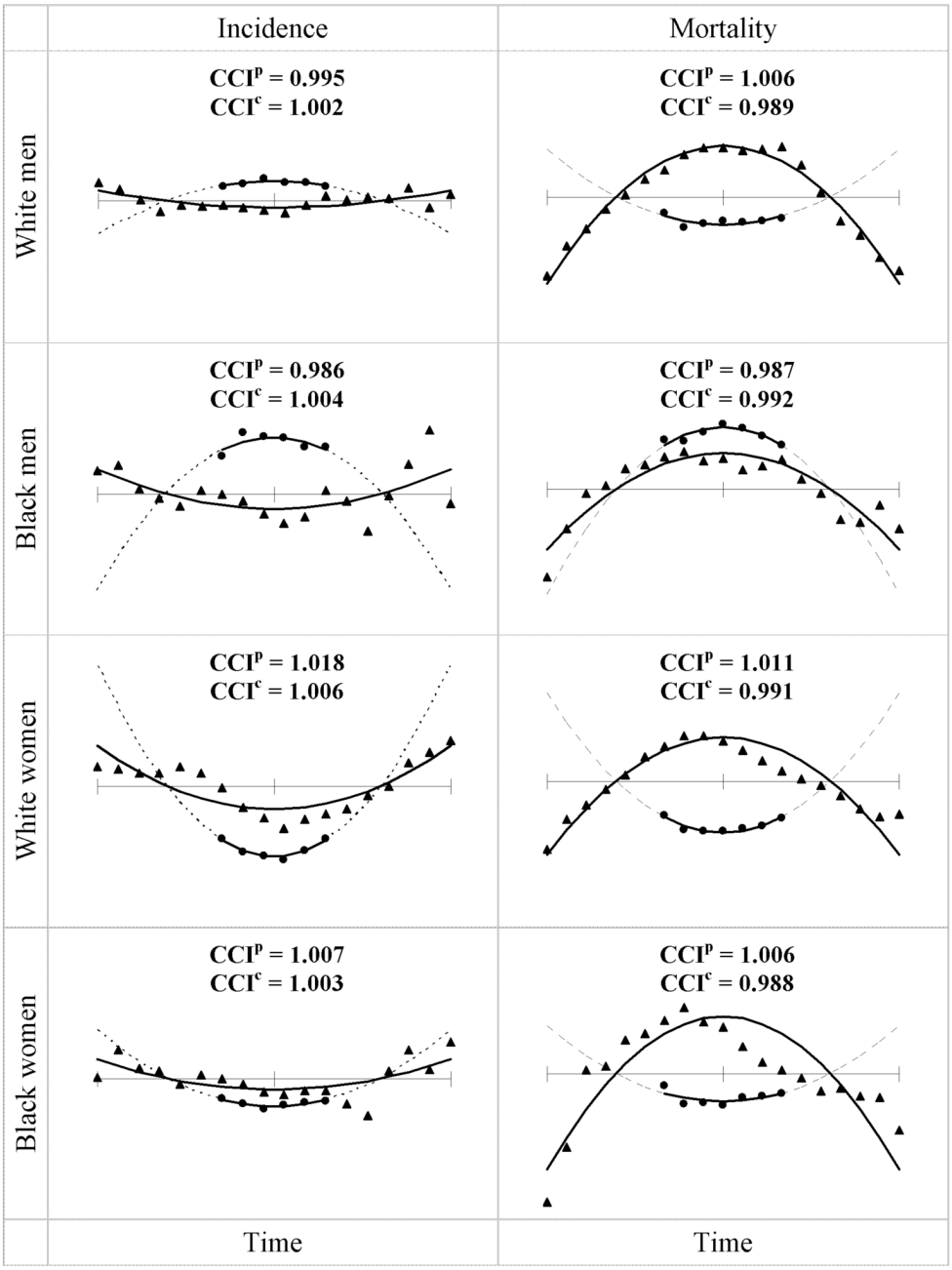

Figure 3.

Time plots of deviations from linear effects under the full APC model (● - time period, ▲ - birth cohort) and the constant-curvature model (solid curves), with deviations measured as vertical distances from the horizontal axis and dashed curves indicating extrapolations to unobserved time periods under the constant-curvature model. Horizontal axes for incidence models span the 1890–1899 through 1975–1984 birth cohorts and 1945–1949 through 2030–2034 time periods. Horizontal axes for mortality models span the 1885–1894 through 1975–1984 birth cohorts and 1940–1944 through 2030–2034 time periods. Each plot includes values for CCI^p (period component of CCI) and CCI^c (cohort component of CCI) (Equation 9, Appendix).

Table

Race- and sex-specific age-period-cohort (APC) analysis of cancer incidence and mortality not related to tobacco, screening, or HIV: Summary measures and statistical significance.

					Statistical significance[2]		
Endpoint	**Group**	**Model[1]**	**AAPC (95% C.I.)**	**CCI (95% C.I.)**	**Test 1**	**Test 2**	**Test 3**
Incidence	White men	Simple	0.88 (0.83, 0.94)	0.997 (0.994, 1.000)	<0.001	<0.001	<0.001
	Black men	Extra	0.12 (−0.11, 0.34)	0.990 (0.977, 1.003)	0.848	0.026	0.062
	White women	Extra	0.69 (0.58, 0.80)	1.023 (1.016, 1.031)	<0.001	<0.001	<0.001
	Black women	Simple	0.52 (0.34, 0.69)	1.010 (1.000, 1.019)	<0.001	0.008	0.177
Mortality	White men	Extra	−0.74 (−0.80, −0.68)	0.995 (0.992, 0.998)	<0.001	<0.001	<0.001
	Black men	Simple	−0.62 (−0.69, −0.55)	0.979 (0.977, 0.981)	<0.001	<0.001	<0.001
	White women	Extra	−0.90 (−0.94, −0.86)	1.002 (1.000, 1.003)	<0.001	<0.001	<0.001
	Black women	Extra	−0.82 (−0.90, −0.74)	0.994 (0.990, 0.997)	<0.001	<0.001	<0.001

AAPC - Average annual percentage change, C.I. - confidence interval, CCI - constant curvature index for 5-year time intervals

[1] Model fitted: simple Poisson model or extra-Poisson model

[2] p-values; Test 1 assesses H_0 AAPC = 0 *vs.* H_A AAPC ≠ 0; Test 2 assesses H_0: constant-curvature model and linear time trend model fit equally well *vs.* H_A constant-curvature model fits better; and Test 3 assesses H_0 full APC model and constant-curvature model fit equally well *vs.* H_A full APC model fits better