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Title: Lung cancer survival in the United States by race and stage (2001–2009): findings from the CONCORD–2 study

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Running title: Lung cancer survival by race and stage

Author's names and academic degrees:

Thomas B. Richards, MD (email: TRichards@cdc.gov)\(^1\)

S. Jane Henley, MSPH (email: SHenley@cdc.gov)\(^1\)

Mary C. Puckett, PhD (email: MPuckett1@cdc.gov)\(^1\)

Hannah K. Weir, PhD (email: HWeir@cdc.gov)\(^1\)

Bin Huang, DrPH, MS (email: bhuang@kcr.uky.edu)\(^2\)

Thomas C. Tucker, PhD, MPH (email: tct@kcr.uky.edu)\(^3\)

Claudia Allemani, PhD (email: Claudia.Allemani@lshtm.ac.uk)\(^4\)

Author's Affiliations:

\(^1\) Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA.

\(^2\) Department of Biostatistics, College of Public Health, University of Kentucky, Lexington, KY

\(^3\) Markey Cancer Center, Kentucky Cancer Registry, and College of Public Health, University of Kentucky, Lexington, KY

\(^4\) Cancer Survival Group, Department of Non-Communicable Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK

Corresponding author: Thomas B Richards, MD, Epidemiology and Applied Research Branch, Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health
Promotion, Centers for Disease Control and Prevention, Bldg 107, F-76, 4770 Buford Highway NE, Atlanta, Georgia 30341-3717, Tel 770-488-3220, Fax 770-488-4286, Email: TRichards@cdc.gov

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ABSTRACT

Background. The second CONCORD study (CONCORD-2) reported that 5-year net survival for lung cancer was low (10%–20%) during 1995–2009 in most countries, including the United States, which was at the higher end of this range.

Methods. Using data from CONCORD-2, we analyzed net survival among lung cancer patients (aged 15–99 years) diagnosed in 37 states, covering 80% of the US population. We corrected survival for background mortality using state- and race-specific life tables, and age-standardized the all-ages estimates using International Cancer Survival Standard weights. We estimated net survival for patients diagnosed during 2001–2003 and 2004–2009 at 1, 3, and 5 years after diagnosis by race (all, black, and white), SEER Summary Stage 2000, and state.

Results. Five-year net survival increased from 16.4% (95% CI, 16.3%–16.5%) in 2001–2003 to 19.0% (18.8%–19.1%) in 2004–2009, with increases in most states and among both blacks and whites. In 2004–2009, 5-year survival was lower among blacks (14.9%) than whites (19.4%), and ranged by state from 14.5% to 25.2%.

Conclusion. Lung cancer survival improved slightly from 2001–2003 to 2004–2009, but was still low, with differences by race and state. Efforts to control well-established risk factors would be expected to have the greatest impact on reducing the burden of lung cancer, and efforts to ensure all patients receive timely and appropriate treatment might reduce the differences in survival by race and state.

Keywords: Lung neoplasms; survival; cancer registries; survival; stage; race; disparities; trends

Précis:
Lung cancer survival improved slightly during 2001–2009, but remained lower among blacks than whites. Efforts to control well-established risk factors would be expected to have the greatest impact on
reducing the burden of lung cancer, and efforts to ensure all patients receive timely and appropriate treatment might reduce the differences in survival by race and state.

**Abbreviations**

NCI, National Cancer Institute; NCCCP, National Comprehensive Cancer Control Program; NPCR, National Program of Cancer Registries; SEER, Surveillance, Epidemiology, and End Results Program.
INTRODUCTION

In the United States, lung cancer accounts for approximately 14% of all invasive cancers diagnosed each year and 27% of all cancer-related deaths.\(^1\) Lung cancer incidence and mortality rates vary by gender and race.\(^1,2\) Among males, lung cancer incidence peaked in 1982, and mortality peaked in 1991.\(^2\) Among females, mortality peaked in 2003, and incidence peaked in 2006.\(^2\) Lung cancer incidence and mortality rates are currently decreasing slowly, but the rates are higher among black males than white males, and lower among black females than white females.\(^1,2\) By 2020, the numbers of lung cancer cases and deaths in the United States are projected to increase because of the aging white population and population growth in the black population.\(^3,4\)

Population-based cancer survival provides an indicator of the overall effectiveness of the health care system to deliver screening, early diagnosis, and evidenced-based treatment services to all people in the population being served.\(^5\) Survival differences between populations may be attributable to disparities in access to early diagnosis and optimal treatment.\(^6\)

The second CONCORD study (CONCORD-2) reported survival for patients with cancer diagnosed from 1995 through 2009 in 67 countries, and enabled the comparison of survival of patients in the United States with other countries.\(^6,7\) The CONCORD-2 study is the largest study to date on lung cancer survival, both in the United States and world-wide. During 1995–2009, the 5-year net survival for patients diagnosed with lung cancer was low in most countries (10% to 20%).\(^6\) Survival in the United States was at the higher end of this range.\(^6\)

In the current study, we conduct a more detailed analysis of the US data from the CONCORD-2 study. We describe and discuss trends in net survival among patients diagnosed with lung cancer by race, stage, and state. We also discuss how population-based lung cancer survival might be used to help inform comprehensive cancer control.\(^8\)
Materials and Methods

Data source

We analyzed the US lung cancer data from the CONCORD-2 study, which included cases reported by 37 state-wide cancer registries that covered approximately 80% of the US population, and that consented to inclusion of their data in the more detailed analyses reported here.7 We analyzed individual tumor records for adults (men and women aged 15–99 years) who were diagnosed with a primary invasive cancer of the lung and bronchus (International Classification of Disease Oncology 3rd edition9 topography codes: C34.0-C34.3; C34.8-C34.9) during 2001–2009, and followed up to December 31, 2009, regardless of whether the patient had had a previous cancer. If a patient was diagnosed with two or more cancers of the lung during 2001–2009, we only considered the first cancer in the survival analyses.


Survival analyses

We analysed net survival by race (all, black, white), by stage (SS2000: localized, regional, distant, unknown), state, and calendar period of diagnosis. We estimated net survival at 1, 3, and 5 years after diagnosis and 95% confidence intervals (CI) using the Pohar Perme estimator.7,12 Net survival can be interpreted as the probability of survival up to a given time since diagnosis, after controlling for other causes of death (background mortality).7 To control for wide differences in background mortality among participating registries, we constructed life tables of all-cause mortality in the general population of each state from the number of deaths and the population, by single year of age, sex, calendar year and, where
possible, by race (black or white), using a flexible Poisson model. These life tables have been published.

We estimated net survival by two different methods, because patients diagnosed in the two calendar periods had different years of follow-up after diagnosis. For patients diagnosed during 2001–2003, we used the cohort approach, since all patients had been followed for at least five years by December 31, 2009. We used the complete approach to estimate net survival for patients diagnosed from 2004–2009, because five years of follow-up data were not available for all patients. We estimated net survival for five age groups (15–44, 45–54, 55–64, 65–74, 75–99 years). We obtained age-standardized survival estimates using the International Cancer Survival Standard (ICSS) weights. If two or more of the five age-specific estimates could not be obtained, we present only the pooled, unstandardized survival estimate for all ages combined. We identify unstandardized state estimates using italics in tables.

An appropriate statistical test is not currently available to evaluate whether two net survival curves differ significantly. We note differences when 95% confidence intervals (CI) for two estimates do not overlap. We also present trends, geographic variations, and differences in age-standardized survival by race in bar charts and funnel plots. Funnel plots of net survival for 2001–2003 and 2004–2009 provide insight into the variability of lung cancer survival by race and state. They show how much a particular survival estimate deviates from the pooled estimate for all registries combined, given the precision of each estimate. We show the pooled estimate of US registries as a horizontal line in the funnel plot.

More details on data and methods are provided in the accompanying article by Allemani et al.

RESULTS
We present the overall results for lung cancer in Tables 1, 2, and 3. We report state-specific results in Supplemental Tables 1, 2, and 3.

**Distribution of cases by stage, race, and calendar period**

A total of 1,404,724 patients were diagnosed with lung cancer during the period 2001–2009; 86.9% were white and 10.2% were black (Table 1). The proportion of patients diagnosed with disease at distant stage increased from 46.8% in 2001–2003 to 50.9% in 2004–2009. In contrast, the proportions of localized stage (17.5% and 17.7%) and regional stage (24.2% and 23.4%) remained relatively stable over time (Table 1). In both time periods, the proportion of blacks diagnosed with localized stage disease was lower than for whites, while a higher proportion of blacks were diagnosed at distant stage. During 2004–2009, the proportion of patients diagnosed at each stage ranged between states as follows: localized (13.1%–21.9%), regional (20.3%–26.3%), and distant (45.4%–59.4%) (Supplemental Table 1).

**1-year, 3-year, and 5-year net survival by race and calendar period**

During 2001–2003, the pooled estimate of net survival of all patients combined was 42.5% (95% CI, 42.4%–42.7%) at 1 year, 21.6% (95% CI, 21.4%–21.7%) at 3 years, and 16.4% (95% CI, 16.3–16.5) at 5 years. For patients diagnosed during 2004–2009, it had risen to 45.6% (95% CI, 45.5%–45.7%) at 1 year, 24.5% (95% CI, 24.4%–24.6%) at 3 years, and 19.0% (95% CI, 18.8%–19.1%) at 5 years (Table 2). Net survival for whites was similar to the overall US net survival at 1, 3, and 5 years, while net survival among blacks was about 4-5% lower than for whites at 1, 3, and 5 years. As the general direction and magnitude of racial disparities were similar at 1, 3 and 5 years, we present only 5-year net survival estimates in the remainder of the results.
Among whites in 37 states in 2004–2009, 5-year net survival ranged by state from 15.1%–25.7% (Supplemental Table 2). Among blacks in 36 states during 2004–2009, 5-year net survival ranged from 7.0%–22.7% (data for 5-year net survival among blacks were not available for Montana).

5-year net survival by stage, race, and calendar period

The pooled estimates of 5-year net survival for the US increased from 50.2% in 2001–2003 to 55.1% in 2004–2009 for localized stage, from 20.2% to 26.4% for regional stage, and from 3.6% to 4.8% for distant stage (Table 3). In both time periods, the US estimate of 5-year net survival was 9–10% lower among blacks than whites for localized stage, and 3–5% lower for regional stage. Among 34 states during 2004–2009, the range in state-specific 5-year net survival was 39.4%–66.4% for patients diagnosed at localized stage, 19.1%–34.0% for regional stage, and 2.8%–10.1% for distant stage (Supplemental Table 3) (5-year survival estimates by stage were not available for Maryland, Wisconsin, or Rhode Island for 2004–2009).


The 5-year net survival in most Northeastern states was higher than the US pooled estimate during both 2001–2003 and 2004–2009 (Figure 1). In contrast, the 5-year net survival in many states in the South, Midwest, and West was lower than the US estimate during both time periods. Between 2001–2003 and 2004–2009, the absolute change in 5-year net survival increased 0.4–6.3% in 35 states, with a small decrease 0.2–0.3% in two states. The absolute increase was greater than 2.6% (the increase in the pooled US estimate) in most states in the Northeast. In contrast, the absolute increase was less than 2.6% in many states in the South, Midwest, and West.

Funnel plots of 5-year net survival by state
Figure 2 shows geographical and racial variation in 5-year net survival by state. Although net survival for lung cancer was generally low in all states, in both calendar periods, survival for black patients was lower than survival for white patients, and in most states it was lower than the pooled estimate of US registries (the horizontal line in the funnel plot).

**Discussion**

This study provided lung cancer survival estimates by race and stage for 37 states including 80% of the US population. During 2004–2009, the US lung cancer 5-year net survival was at the high end of the range for many countries in the CONCORD-2 study, and consistent with 5-year relative survival estimates previously reported in NPCR and SEER registries.

Even for a lethal cancer such as lung cancer, survival for blacks was lower than for whites and this was true especially for localized cancer for which surgery is the main treatment of curative intent. We found that the overall 5-year net survival for lung cancer (19.0%) was 4.2% higher than for liver cancer (14.8%), but lower than the net survival for the other cancers included in this Supplement: stomach (29.0%), ovary (41.0%), cervix (62.8%), rectum (64.0%), colon (64.6%), acute lymphoblastic leukemia in children (88.1%), breast (88.6%), and prostate (96.9%) cancer.

In 2004–2009, we found 5-year net survival for all stages was 4.5% lower among blacks than among whites. The racial differences were even more marked for lung cancer diagnosed at a local stage (9.9% lower among blacks), 4.7% lower among blacks diagnosed at regional stage, but essentially the same for patients diagnosed at a distant stage (only 0.3% lower among blacks). Our results are consistent with other reports of racial disparities in lung cancer. Reviews suggest that the reasons for the wide racial disparities in lung cancer survival are complex and multifactorial, with contributions from treatment-related factors such as physician-patient encounters and decision making, and barriers to access to high-quality care such as lower patient income or insurance coverage limits. Unfortunately,
although our study highlights two key determinants (race and stage) of survival differences between US states, it does not provide definite conclusions about all the factors that may contribute to differences, because information on all factors is not available for all cancer patients at a population-based level. It would be interesting to analyze the availability of optimal treatment by US state and race. This may be possible during the next cycle of CONCORD (CONCORD-3).

In most states, we observed small but consistent increases in 5-year lung cancer net survival from 2001–2003 to 2004–2009, even though the study only covers a single decade. Overall, the increase in 5-year net survival among whites was 2.6%, while the increase in blacks was 1.8%. We also observed considerable variation in lung cancer survival between US states. Overall, 5-year net survival ranged widely by state from 14.5% to 25.2% during 2004–2009, and ranges in survival were more extensive by stage: 39.4%–66.4% for patients diagnosed at localized stage, 19.1%–34.0% for regional stage, and 2.8%–10.1% for distant stage. We also observed that the change in survival between the two time periods ranged by state, from decreased survival in 2 states to an increase of up to 6.3% in the other 35 states. As with differences by race, our study does not enable definite conclusions about the explanation for the differences we observed over time and by geography.

Clinical perspective

During 2001–2009, a number of improvements occurred in clinical care for lung cancer; for example, increased use of video-assisted thoracic surgery, intensity modulated radiation therapy, and targeted therapy, also referred to as precision or personalized treatment. We could not directly assess whether differential access to treatment by race contributed to the racial disparities in survival, because we did not have data on the treatment received by each patient, but “if equal treatment [for lung cancer] yields equal outcome regardless of race”, that is a plausible conclusion.
Survival can be improved if treatment can be provided when lung cancer is diagnosed at a localized stage.\textsuperscript{35,38} For the cancers in this Supplement, only patients diagnosed at a localized stage with liver cancer had lower 5-year survival (25.7\%)\textsuperscript{18} during 2004–2009 than for lung cancer at localized stage (55.1\%). In contrast, cancers commonly identified through screening tests (colon, breast and prostate cancers) had the highest 5-year survival for localized stage during 2004–2009, at 89.7\%,\textsuperscript{23} 98.3\%,\textsuperscript{25} and 99.9\%,\textsuperscript{26} respectively. For the other cancers in this Supplement, only ovarian cancer had a higher proportion of cases (56.8\%)\textsuperscript{20} diagnosed at a distant stage during 2004–2009 than lung cancer (50.9\%). Cancers commonly identified through screening tests (colon, breast and prostate cancers) during 2004–2009 had lower proportions of cases diagnosed at a distant stage, at 19.3\%,\textsuperscript{23} 5.2\%,\textsuperscript{25} and 3.7\%,\textsuperscript{26} respectively.

Screening with low dose-computed tomography (CT) is now recommended by the US Preventive Services Task Force (USPSTF)\textsuperscript{39} for individuals at high risk for lung cancer, and is covered by Medicare.\textsuperscript{40} However, early detection of lung cancer by screening is unlikely to have contributed to the increase in 5-year net survival that we observed for lung cancer, because low dose CT scan was not broadly available or recommended during 2001–2009,\textsuperscript{41} and the USPSTF recommendations and Medicare regulations were only issued later.

In our study, the overall proportion of cases with unknown stage decreased from 11.5\% in 2001–2003 to 8.0\% in 2004–2009. This is an encouraging finding because accurate lung cancer staging\textsuperscript{35} is needed to guide therapy selection. Although this decrease is consistent with an increase in accuracy over time in lung cancer staging, the observed changes could be an artifact related to changes in staging methods between the two calendar periods. Alternatively, cases with unknown stage could be missing at random where some centers did not provide the data; the overall survival for these cases likely would be similar to the average survival for all cases. Cases with unknown stage also could reflect data from patients not completely staged because they were not good candidates for clinical workup and treatment;
the overall survival for these cases would be similar to cases with a more advanced stage. In 2004–2009, the survival for cases with unknown stage in our study was lower than the survival for local or regional stage, but higher than the survival for distant stage; this pattern suggests that many of the unknown cases were likely similar to cases with a more advanced stage.

**CDC Cancer Prevention and Control Programs**

The National Comprehensive Cancer Control Program (NCCCP) supports state, tribal, and territory programs to develop cancer plans that design and implement activities in cancer prevention and control.\(^8\)\(^,\)\(^4\)\(^2\) State-specific data are critical to inform these cancer control plans and activities.

While research is conducted to improve clinical care and to reduce racial disparities, the greatest impact to reduce lung cancer incidence will come from cancer control efforts directed at primary prevention of established risk factors, such as cigarette smoking,\(^4\)\(^3\) the inhalation of secondhand smoke by nonsmokers,\(^4\)\(^3\) indoor radon (a leading cause of lung cancer among non-smokers),\(^4\)\(^4\) occupational exposures to carcinogens,\(^4\)\(^5\) and air pollution.\(^4\)\(^5\)

To address lung cancer prevention, mortality, and survival, NCCCP programs develop detailed plans to prevent and control cancer for their communities, and the majority include objectives for reducing tobacco use and indoor radon exposure. For example, two-thirds of NCCCP programs include funding for tobacco control, such as supporting cessation services and smoke-free policies.\(^4\)\(^6\) NCCCP programs work with a national network of partner organizations to reach populations that tend to be heavy smokers.\(^4\)\(^7\) Continued and expanded access to tobacco cessation services could increase abstinence rates and decrease lung cancer incidence further.

Several NCCCP programs support activities related to lung cancer screening, including awareness through health care provider education, media campaigns, and surveys to better understand the status of lung cancer screening in their communities.\(^4\)\(^8\) Continued and expanded incorporation of
objectives related to USPSTF lung cancer screening recommendations into NCCCP cancer plans could increase early detection of lung cancer, thereby improving lung cancer survival. NCCCP programs could utilize their experiences from other cancer screening programs to impact lung cancer screening rates at a population level. Further, as lung cancer screening begins to be fully implemented in the United States, NCCCP programs might explore the use of patient navigators to coordinate and improve compliance with follow-up visits and annual repeated lung cancer screening.

In the future, NCCCP programs also might consider the feasibility of monitoring and evaluating the quality of diagnostic, treatment, and survivorship services for patients with lung cancer. By improving understanding of lung cancer care and whether advances in care are differentially accessed, NCCCP programs may identify effective ways to improve lung cancer survival and reduce disparities in various communities.

NCCCP programs can use lung cancer net survival estimates for their states as an additional data resource to support cancer prevention and control. Combined with data on cancer incidence and death rates, cancer survival measures can provide a more comprehensive picture of the burden of cancer in a population and support public health efforts to reduce cancer health disparities.

**Strengths and Limitations**

The overview paper by Weir et al. for this Supplement describes the strengths and limitations that apply to all of the papers in this Supplement, including this analysis of lung cancer survival.

**Conclusions**

We found that lung cancer survival improved slightly from 16.4% in 2001–2003 to 19.0% in 2004–2009 in the United States overall and in most states. It was low even for localized stage (55.1%) in 2004–2009, and was even lower among blacks (14.9%) than whites (19.4%). We also observed considerable
variation (14.5% to 25.2%) in state-specific lung cancer survival in 2004–2009. During 2001–2009, lung cancer incidence and mortality in the United States decreased slowly.\textsuperscript{1,2} Lung cancer mortality trends mirror lung cancer incidence trends because of the high fatality rate and low survival for patients with lung cancer.\textsuperscript{5} Given the low survival observed in all states, cancer control efforts directed at primary prevention through control of well-established risk factors would be expected to have the greatest impact on reducing the burden of lung cancer in the long term. Efforts directed at improving equality of access to treatment would be expected to reduce the racial differences in survival in the short to medium term.

References


Table 1. Lung cancer: number of cases (males and females aged 15-99 years) diagnosed 2001–2009 and distribution (%) by SEER Summary Stage 2000 at diagnosis, by race and calendar period of diagnosis.

<table>
<thead>
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<td>Black</td>
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<td>393,257</td>
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<td>Regional (%)</td>
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<td>24.2</td>
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<tr>
<td>Distant (%)</td>
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<td>50.9</td>
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<tr>
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<td>11.5</td>
<td>11.7</td>
<td>10.6</td>
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Note: SEER = Surveillance, Epidemiology and End Results (SEER) Program. Information on stage was not available for two states (Maryland and Wisconsin), or for Rhode Island for cases diagnosed during 2004–2009.
Table 2. Lung cancer: age-standardized net survival (%) at 1, 3 and 5 years for cases (males and females aged 15-99 years) diagnosed 2001–2009, by race and calendar period of diagnosis.

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<td></td>
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<td>95% CI</td>
<td>NS (%)</td>
<td>95% CI</td>
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<td>21.6</td>
<td>21.4 - 21.7</td>
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<tr>
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<td>16.4</td>
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<td>16.8</td>
<td>16.6 - 16.9</td>
<td>13.1</td>
<td>12.8 - 13.5</td>
</tr>
</tbody>
</table>

NS = net survival
CI = confidence interval

Note: Unstandardized estimates are italicized.
Table 3. Lung cancer: 5-year age-standardized net survival (%) for adult cases (males and females aged 15-99 years) diagnosed 2001–2009, by SEER Summary Stage 2000 at diagnosis, race, and calendar period of diagnosis.

<table>
<thead>
<tr>
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<tbody>
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<td></td>
<td>All races</td>
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<td></td>
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<tr>
<td>Regional</td>
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<td>Distant</td>
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<tr>
<td>Unknown</td>
<td>13.0</td>
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</table>

NS = net survival
CI = confidence interval
SEER = Surveillance, Epidemiology and End Results (SEER) Program
Figures

Figure 1. Lung cancer: 5-year age-standardized net survival (%) for adult cases (males and females aged 15–99 years) diagnosed with lung cancer during 2001–2003 and 2004–2009, and the absolute change (%). States are grouped by US Census Region.

Note: States are ranked within Census Region by the survival estimate for 2004–2009.

Note: Dark colors – states affiliated with the National Program of Cancer Registries (NPCR); pale colors – states affiliated with the Surveillance, Epidemiology and End Results (SEER) Program. *Registries affiliated with both federal surveillance programs. Change (%) not plotted because at least one calendar period estimate was not age-standardized.

Figure 2. Lung cancer: 5-year age-standardized net survival (%) for adult cases (males and females aged 15–99 years), by state, race, and calendar period of diagnosis.

Note: The pooled (US) survival for each calendar period is shown by the horizontal (solid) line with corresponding 95.0% and 99.8% control limits (dotted lines).
Supplemental Tables

Supplemental Table 1. Lung cancer: number of adult cases (males and females aged 15–99 years) during 2001–2009, and the distribution (%) by SEER Summary Stage 2000 at diagnosis, race, calendar period, and US Census Region, Division, and states.

Note: NPCR indicates National Program of Cancer Registries; SEER indicates Surveillance, Epidemiology and End Results (SEER) Program. Information on stage was not available for two states (Maryland and Wisconsin), or for Rhode Island for cases diagnosed during 2004–2009.

Supplemental Table 2. Lung cancer: age-standardized net survival (%) at 1, 3 and 5 years for cases (males and females aged 15–99 years) diagnosed during 2001–2009, by race, calendar period of diagnosis, and US Census Region, Division, and states.

Note: NPCR indicates National Program of Cancer Registries; SEER indicates Surveillance, Epidemiology, and End Results program. Unstandardized estimates are italicized.

Supplemental Table 3. Lung cancer: 5-year age-standardized net survival (%) for adult cases (males and females aged 15–99 years) diagnosed during 2001–2009, by SEER Summary Stage 2000 at diagnosis, race, calendar period, and US Census Region, Division, and states.

Note: NPCR indicates National Program of Cancer Registries; SEER indicates Surveillance, Epidemiology, and End Results program. Information on stage was not available for two states (Maryland and Wisconsin), or for Rhode Island for cases diagnosed during 2004–2009. Unstandardized estimates are italicized.