ABSTRACT: **Context:** Composed of all or a portion of 13 states, Appalachia is a heterogeneous, economically disadvantaged region of the eastern United States. While mortality from cancer in Appalachia has previously been reported to be elevated, rates of cancer incidence in Appalachia remain unreported. **Purpose:** To estimate Appalachian cancer incidence by stage and site and to determine if incidence was greater than that in the United States. **Methods:** Using 1994–1998 data from the central registries of Kentucky, Pennsylvania, and West Virginia, age-adjusted incidence rates were calculated for the rural and nonrural regions of Appalachia. These state rates were compared to rates from the Surveillance, Epidemiology, and End Results (SEER) program for the same years by calculating the adjusted rate ratio (RR) and a 95% confidence interval (CI). **Findings:** Both the entire and rural Appalachian regions had an adjusted incidence rate for all cancer sites similar to the SEER rate (RR = 1.00 [95% CI, 1.00–1.01] and RR = 0.99 [95% CI, 0.99–1.00], respectively). However, incidence of cancer of the lung/bronchus, colon, rectum, and cervix in Appalachia was significantly elevated (RR = 1.22 [95% CI, 1.20–1.23], 1.13 [95% CI, 1.11–1.14], 1.19 [95% CI, 1.16–1.22], and 1.12 [95% CI, 1.07–1.17], respectively). Incidence of cancer of the lung/bronchus and cervix in rural Appalachia was even more elevated (RR = 1.34 [95% CI, 1.31–1.36] and 1.29 [95% CI, 1.21–1.38], respectively). Incidence of unstaged disease for all cancer sites in Appalachia (RR = 1.06 [95% CI, 1.05–1.08]), particularly rural Appalachia (RR = 1.28 [95% CI, 1.25–1.30]), was elevated. **Conclusions:** Cancer incidence in Appalachia was not found to be elevated. However, incidence of cancer of the lung/bronchus, colon, rectum, and cervix was elevated in Appalachia. The rates of unstaged cancer of every examined site were elevated in rural Appalachia, suggesting a lack of access to cancer health care.

Cancer Incidence in Kentucky, Pennsylvania, and West Virginia: Disparities in Appalachia

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However, the incidence of cancer in Appalachia has not been studied extensively, so it is largely unknown if the incidence of cancer is elevated similar to mortality. In one of the few publications to specifically examine incidence in this region, invasive cervical cancer in an Appalachian region of Kentucky was found to be nearly twice the incidence recorded by the registries of the Surveillance, Epidemiology, and End Results (SEER) program of the NCI; carcinoma in situ of the cervix was 21% higher in Appalachia than that found in SEER. Thus, both the incidence of and the mortality from cervical cancer appear to be elevated in Appalachia; comparisons of incidence and mortality for other cancer sites are limited. Knowledge of cancer incidence is important because it may suggest interventions that would not be obvious by examination of mortality data only.

Appalachia is largely rural—2 of every 3 Appalachian counties are rural, and 1 in 3 persons in Appalachia reside in a rural county. The effect of rurality, a key characteristic of Appalachia, on all cancer incidence has not been consistently reported in the literature, though most publications report that incidence is higher in urban regions than in rural regions. In a review of published research since 1950, age-, race-, and sex-adjusted incidence for all cancer was concluded to be generally higher in urban than in rural regions. Since the publication of that review in 1992, an increasing rural-to-urban gradient has been reported for all cancer incidence in Texas and Illinois. However, no urban/rural difference for all cancer incidence was found in Mississippi.

For specific cancer sites, the rural-to-urban gradient in cancer incidence has been more variably reported. Among women, some rural/urban studies found higher rates of cervical cancer in rural areas, and other studies found higher rates in urban areas. Generally, the incidence of breast cancer has been reported to be lower in rural areas than in urban areas, however, no rural/urban difference was observed for breast cancer incidence in the San Francisco Bay Area and Mississippi. For lung cancer, incidence in rural areas has been lower than that in urban areas, especially for white females. Similarly, incidence of colorectal cancer for white males has been lower in rural areas than urban areas.

When compared to residents of urban areas, residents of rural areas of the United States and northern Europe have been shown to have had all cancers—as well as cancers of the cervix, lung or lung/bronchus, colon/rectum, and female breast—diagnosed more frequently at a late stage. In Mississippi and Georgia, rural residents were more likely than urban residents to have had unstaged tumors. Diagnosis at a late stage and failure to have a tumor staged have been associated with poorer survival from cancer. Consequently, residents of rural regions, including those in Appalachia, may have experienced poorer survival after diagnosis of cancer than would have residents of nonrural regions.

The purpose of this study was to characterize cancer incidence in Appalachia—a geographic area with elevated cancer mortality—with particular attention to its rural region. Specifically, this study (1) estimated incidence by stage at diagnosis for this area, (2) estimated incidence and stage at diagnosis for residents of the rural and nonrural regions of Appalachia, and (3) compared these rates to similar estimates for the United States. This description of cancer incidence can lead to hypotheses related to access to cancer early detection, utilization of care or treatment, and survival in Appalachia and its rural region.

**Methods**

The Appalachia Cancer Network (ACN), is a member of the Special Populations Network, is one of NCI’s current initiatives in Appalachia. ACN partners with academic, government, health, and community organizations to conduct cancer control research that improves the availability, utilization, and effectiveness of cancer screening and educational services in 8 states of Appalachia. To facilitate cancer surveillance, ACN established the Surveillance Task Force (STF), which is composed of academic researchers and representatives of the central cancer registries of Kentucky (KY), Pennsylvania (PA), and West Virginia (WV).

The central registries of KY, PA, and WV provided the STF with data on histologically confirmed cancer cases diagnosed among their residents between January 1, 1994, and December 31, 1998 (n = 509,593). Data for each case included date of diagnosis, race, gender, county of residence at diagnosis, primary cancer site, and general summary stage. Data from the 11 registries of NCI’s SEER program for the same time period were used for comparison. SEER covered approximately 14% of the US population during the time period, including state registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah. Cases of in situ disease were excluded from both the Appalachian (n = 17,393) and SEER data.

Using SEER coding categories, cases were grouped into 5 specific cancer sites based on the primary site of tumor origin: lung/bronchus (ICD-O-2 C34.0–C34.9), colon (C18.0–C18.9, C26.0), rectum (C19.9, C20.9), female breast (C50.0–C50.9), and cervix uteri (C53.0–C53.9). SEER summary stage of disease
was used to characterize stage at diagnosis into 4 categories of invasive disease: local, regional, distant, and unstaged. Local tumors were those confined to the organ of origin. Cases of regional stage disease included tumors that had spread by either direct extension to immediately adjacent tissues or organs or into lymph nodes regional to the primary site of origin. Tumors that had regionally spread but for which the extent of regional spread could not be determined or was not specified were also considered regional stage disease. Tumors that had spread and developed secondary or metastatic tumors, had seeding or implants, or were systemic were considered distant stage disease. Unstaged disease was defined by those cases where not enough information was available to accurately determine stage.

The county of residence at the time of diagnosis was used to classify each patient as a resident of the Appalachian area of the 3 states and as a resident of a rural county in the Appalachian area (the Figure). Counties were categorized as Appalachian or non-Appalachian in accordance with the Appalachia Regional Commission’s designation (406 counties in October 2001). West Virginia was entirely within Appalachia (n = 55 counties). In eastern Kentucky, 49 counties were Appalachian, while in Pennsylvania all counties except those in the southeastern corner of the state were Appalachian (n = 52). Reports of cancer patients with an unknown county of residence (n = 2) or a county of residence not in Appalachia (n = 252,528) were excluded from the KY, PA, and WV data. Additional analyses were also performed on data from the rural counties within Appalachia (referred to herein as “rural” or “rural Appalachia”). Rural status was assigned to Appalachian counties with codes 6 to 9 of the US Department of Agriculture (USDA) 1993...
Rural-Urban Continuum Codes\textsuperscript{26} (frequently reported as Beale codes); nonrural counties were those with codes 0 to 5. Under this definition, rural counties were those nonmetropolitan counties with urban populations of less than 20,000. For the denominator, 1994–1998 county-specific population estimates were obtained from SEER.\textsuperscript{27}

To quantify relative incidence, we age-adjusted incidence rates to the year 2000 US standard million population by the direct method and reported them per 100,000 population. Standard errors and 95% confidence intervals were calculated.\textsuperscript{28} Rate ratios (RR) and their corresponding 95% confidence intervals were also calculated.\textsuperscript{29} We particularly discuss the incidence of local and unstaged cancer because of their importance as measures of screening and access to cancer health care, respectively. SAS version 8.0 (SAS Inc, Cary, NC) and SEER*Stat version 4.2 were used for analysis. This research was approved by the Institutional Review Board, Pennsylvania State University College of Medicine, on July 17, 2001, Protocol 2001-215EM.

### Results

**Appalachian Region.** From 1994 to 1998, 8.7 million people resided in the 156 Appalachian counties of KY, PA, and WV; 95.4\% were white, 3.9\% black, and 0.8\% of other races (Table 1). Approximately 2.8 million people (32\%) resided in the 110 rural counties; 98.0\% of the population was white.

From 1994 to 1998, the incidence of all cancer in the Appalachian region was 471.7/100,000 (n = 239,670) (Table 2). The rural and nonrural regions of Appalachia had relatively similar rates (468.3/100,000 and 473.1/100,000, respectively). When compared to the nonrural region, the rural region had a lower rate of local stage cancer but had a higher rate of unstaged cancer.

The incidence of lung cancer in the Appalachian region was 77.6/100,000 (n = 40,408). The rural region had a higher rate (85.4/100,000) than did the nonrural region (74.2/100,000). When compared to the nonrural region, the rural region had a similar rate of local stage cancer but had a substantially higher rate of unstaged cancer.

The incidence of colon cancer in the Appalachian region was 44.1/100,000 (n = 22,956). The rural region had a lower rate (42.0/100,000) than did the nonrural region (44.9/100,000). When compared to the nonrural region, the rural region had a lower rate of local stage cancer but had a higher rate of unstaged cancer.

The incidence of rectal cancer in the Appalachian region was 17.6/100,000 (n = 9066). As with colon cancer, the rural region had a lower rate (16.5/100,000) than did the nonrural region (18.1/100,000). When compared to the nonrural region, the rural region had a lower rate of local stage cancer and had a similar rate of unstaged cancer.

The incidence of female breast cancer in the Appalachian region was 121.9/100,000 (n = 33,184). The rural region had a lower rate (113.3/100,000) than did the nonrural region (125.7/100,000). When compared to the nonrural region, the rural region had a lower rate of local stage cancer but had a higher rate of unstaged cancer.

The incidence of cervical cancer in the Appalachian region was 11.3/100,000 (n = 2722). The rural region had a higher rate (13.1/100,000) than did the nonrural region (10.6/100,000). When compared to the nonrural region, the rural region had a higher rate of local stage cancer and also had a higher rate of unstaged cancer.

### Comparison to SEER.

For 1994–1998, the rates of incident cancer in the Appalachian region and the rural Appalachian region were equivalent to the SEER rate (RR = 1.00 and 0.99, respectively). However, the rates of local stage cancer in Appalachia and rural Appalachia were lower than the SEER rate (RR = 0.97 and 0.92, respectively). Conversely, the rates of unstaged cancer in Appalachia and rural Appalachia were higher than the SEER rate (RR = 1.06 and 1.28, respectively).

For lung cancer, the incidence in Appalachia and rural Appalachia was greater than that in SEER (RR = 1.22 and 1.34, respectively). The rates of local stage cancer in Appalachia and rural Appalachia were substantially higher than the SEER rate (RR = 1.61 and 1.63, respectively), and the rates of unstaged cancer in Appalachia, and especially in rural Appalachia, were.

### Table 1. Characteristics of the Appalachian Region of KY, PA, and WV, 1994–1998

<table>
<thead>
<tr>
<th></th>
<th>Appalachian Region</th>
<th>Rural Appalachian Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population*</td>
<td>8,709,353 100</td>
<td>2,809,026 100</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
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<tr>
<td>White</td>
<td>8,307,025 95.4</td>
<td>2,751,506 98.0</td>
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<tr>
<td>Black</td>
<td>336,137 3.9</td>
<td>44,250 1.6</td>
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<tr>
<td>Other</td>
<td>66,191 0.8</td>
<td>13,270 0.5</td>
</tr>
<tr>
<td>Counties</td>
<td>156</td>
<td>110</td>
</tr>
</tbody>
</table>

* Average annual population as reported in Surveillance, Epidemiology, and End Results (SEER) county population files for 1994–1998.
higher than the SEER rate (RR = 1.06 and 1.53, respectively).

For each colon and rectal cancer, the incidence rate in Appalachia was greater than that in SEER (RR = 1.13 and 1.19, respectively), as were the incidence rates in rural Appalachia (RR = 1.07 and 1.11, respectively). The rates of local stage colon and rectum cancer in Appalachia were higher than the SEER rates (RR = 1.12 and 1.09, respectively), while the rates of local stage colon and rectum cancer in rural Appalachia were equivalent to the SEER rates (RR = 1.01 and 0.98, respectively). The rates of unstaged colon and rectum cancer in Appalachia were higher than the SEER rates (RR = 1.43 and 1.40, respectively).

Lengerich et al. Winter 2005
For females, the incidence of breast cancer in Appalachia was less than that in SEER (RR = 0.92); however, the rate ratio for rural Appalachia/SEER was even lower (RR = 0.85). The rates of local stage cancer in Appalachia and rural Appalachia were lower than the SEER rate (RR = 0.90 and 0.80, respectively). However, the rate of unstaged cancer in Appalachia was similar to the SEER rate (RR = 0.98), while the unstaged rate in rural Appalachia was higher than the SEER rate (RR = 1.36).

For cervical cancer, the Appalachia/SEER rate ratio was 1.12, while the rate ratio for rural Appalachia/SEER was even higher (RR = 1.29). The rates of local stage cancer in Appalachia and rural Appalachia were higher than the SEER rate (RR = 1.17 and 1.30, respectively) and the rates of unstaged cancer in Appalachia, and especially in rural Appalachia, were higher than the SEER rate (RR = 1.09 and 1.62, respectively).

Discussion

Appalachia. While this study found similar incidence for all cancer sites combined in the Appalachian and SEER populations, incidence of lung, colon, rectal, and cervical cancer was each substantially higher in Appalachia than in SEER. We found also that for each of these same cancer sites, the rate for each local stage and unstaged disease was higher in Appalachia than in SEER. These results are consistent with previous studies that reported higher cancer mortality in Appalachia. However, the incidence rate ratios in this study were further from unity than were mortality ratios. This observation might be a result of methodological differences between the studies. For example, cancer mortality in all of Appalachia was compared to mortality for all of the United States, while the present study compared incidence in only the Appalachian area of KY, PA, and WV to the 14% of the US population covered by SEER during the study period.

Rural Appalachia. Within rural Appalachia, the rate of cancer incidence at all sites was similar to that found in SEER. However, incidences of lung and cervical cancer were especially elevated in the rural region. This finding suggests that risk factors for certain cancers may be higher in rural areas than in nonrural areas and reinforces the need to examine the rural/urban relationship for specific types of cancer rather than for all sites combined.

In addition, the rate of unstaged cancers at all sites, as well as at each of the specific sites examined, was particularly elevated for rural Appalachia. This finding suggests that rural residents diagnosed with cancer may not have received comprehensive diagnostic or treatment services. Patient-related reasons that might cause cancer to remain unstaged after diagnosis include patient choice, financial constraints, or the lack of access to comprehensive services. In addition, reporting procedures may affect the rate of unstaged cancer if, for example, a health care institution diagnoses cancer in a patient but does not complete staging because the patient received a final diagnosis at another institution or at a later date. Greater patient distance to a cancer center has been associated with poorer cancer survival. Such may be the case in rural Appalachia.

Lung Cancer. When compared to SEER, lung cancer incidence was elevated for Appalachia, especially for rural Appalachia. Rates in Appalachia were notably elevated for cancers diagnosed at a local stage and for unstaged disease. Similar to mortality findings, lung cancer incidence in rural Appalachia was particularly elevated for males, while for females the ratio was lower but still elevated. Tobacco use is a primary risk factor for lung cancer, and the states of KY and WV have consistently had the highest prevalence of adult smoking in the United States, which is likely to contribute to the increase in incidence. In addition, coal mining, which is an occupation of many people, particularly among men, in eastern KY and WV, may be a risk factor for lung cancer.

Colon and Rectal Cancer. While the overall rates of colon and rectal cancer were similar in the rural and nonrural Appalachian regions, both were greater than that found in SEER. Also, the relatively low rate of local stage disease suggests decreased utilization of colorectal cancer screening in Appalachia, a geographic area with elevated colorectal cancer mortality. In addition, access to and utilization of diagnostic and treatment services for colon and rectal cancer may be reduced because incidence of unstaged colon and rectal cancer in rural Appalachia was substantially elevated.

Female Breast Cancer. We found that female breast cancer incidence in the Appalachian area and the rural Appalachian region was lower than that found in SEER. This reduced breast cancer incidence was largely attributable to the lower rate of diagnosis at local (and regional) stage and is consistent with a previously reported 3% lower prevalence of breast cancer screening in Appalachia. The rate of unstaged (and distant stage) female breast cancer in the rural region was greater than the rate from SEER. An elevated ratio for unstaged (and distant stage) breast cancer may indicate lower utilization of early detection, diagnostic, and treatment services for breast cancer. Decreased utilization of...
breast-conserving surgery by breast cancer patients has been found in an Appalachian area of Kentucky.  

**Cervical Cancer.** Despite similar rates for distant stage disease, rates of invasive cervical cancer, as well as rates for local (and regional) stage at diagnosis, were especially elevated in rural Appalachia. Elevated cervical cancer incidence in Appalachia has been previously reported, and cervical cancer mortality has been found to be greater than in other areas of the United States. Elevated rates of local (and regional) stages at diagnosis may suggest elevated prevalence of risk factors, including reduced Pap screening, elevated prevalence of high-risk human papilloma virus, multiple sexual partners, and tobacco use. Like breast cancer screening, cervical cancer screening has been found to be about 3% less in Appalachia than in the remainder of the United States. A high rate of tobacco use among women with cervical cancer has been reported in Appalachia.

**Limitations and Future Issues.** There are several limitations to this study. First, designation of rural status was made at the county level, which may have introduced misclassification of individual cases and population. This method has been used previously for cancer research, although alternative rural classification schemes—including population density, distance to cancer treatment center, distance/time to cancer center, size of largest city within a county, county population, town population, municipality code, and ZIP code/census tract—have been used. Additionally, we were not able to identify specific risk factors of Appalachia or rurality that may have affected incidence.

Second, demographic differences were observed between the Appalachian population and the SEER reference population. The Appalachian area had a substantially smaller black population than did the SEER area (3.9% vs 10.9%, respectively), and an even smaller percentage of residents in rural Appalachia were black (1.6%). Within SEER, the black population experienced a greater rate of cancer incidence than did the white population (RR = 1.10); for Appalachia, the black/white rate ratio was 1.05. While the Appalachian sample was too small to stratify for analysis by site or stage, the age-adjusted rate of reported cancer incidence among blacks in Appalachia and rural Appalachia was 489.7/100,000 (95% CI, 478.3–501.1) and 452.8/100,000 (95% CI, 422.9–482.7), respectively, compared to SEER’s rate of 522.6/100,000 (95% CI, 518.7–526.5).

Demographic differences in these populations were also seen in persons of other races. Appalachia has a lower percentage of persons of other races than does SEER (0.8% vs 11.4%, respectively), and, within SEER, persons of other race experienced less cancer than did whites (RR = 0.71). The net effect of the differences in demographics between Appalachia and SEER is unclear because having a smaller percentage of blacks (a high-rate group) in Appalachia could have reduced the Appalachian rate, while having a smaller percentage of other races (a low-rate group) could have elevated the Appalachian rate.

Third, while it is possible that case ascertainment for the state registries may have been incomplete, this is unlikely. During 1998, each of the participating registries was designated by the North American Association of Central Cancer Registries (NAACCR) as meeting the highest certification standard based on evaluation of 6 criteria that reflect the ability to produce complete, accurate, and timely data.

Fourth, this analysis was conducted with data from the Appalachian area of 3 contiguous states. However, Appalachia is not a homogeneous region. For example, unique statewide public health or education programs that effectively promote prevention or early detection could affect cancer incidence. Beyond these programs, characteristics of each state’s population could also influence cancer risk (eg, smoking prevalence, occupation).

Finally, age adjustment in the current study used the 2000 US population standard rather than the 1970 population standard commonly used in previous reports of cancer mortality and incidence. Because the 2000 US standard weights older age-groups more than previous US population standards and because cancer rates increase with age, adjusted rates of cancer in this study may be greater than rates reported previously. However, the effect on rate ratios that use the same standard for both the numerator and the denominator should be negligible.

Despite these considerations, this study is significant because it is the first of which the authors are aware to report cancer incidence from 3 contiguous Appalachian states engaged in a single research and delivery program focused on prevention and control of cancer at several sites. Such a report is possible only because of similar, high-quality data collected by the central registries of each of the 3 participating states. These and other state registries have received valuable assistance for public health surveillance from NAACCR, CDC’s National Program of Cancer Registries, and NCI’s SEER Program. These programs, along with common standards for chronic disease surveillance, enable state-collected data to be used collectively to examine regional health issues.

The findings from this study suggest several future analyses. First, a better understanding of both the
geographic distribution of unstaged cancers and the characteristics of patients with unstaged cancer, especially within the rural Appalachian region, will better portray risk of cancer death. Second, regional differences in stage-specific cancer incidence may partly result from differences in screening rates. Analysis of stage at diagnosis, with inclusion of in situ cases, has been used previously as a surrogate marker for breast cancer screening and may prove useful in Appalachia as well. Third, examination of incidence/mortality ratios or survival rates by stage at diagnosis may suggest differences in treatment patterns within Appalachia. Fourth, state- or substate-specific analyses may explore differences in incidence rates by state. To pursue surveillance analyses such as these, the Appalachia Cancer Network (ACN) Surveillance Task Force will provide data to non-ACN investigators whose proposals are approved by representatives of each of the 3 states on the STF and the proposing investigator’s local institutional review board.

Finally, specific characteristics of individual patients in Appalachia should be examined, possibly through retrospective case-control study designs. Such analytic studies may identify risk factors and be less susceptible to ecological fallacy than surveillance studies. In addition, such studies may lead to interventions for the Appalachian population that can be implemented by academic, governmental, and volunteer groups.

Appalachia is an excellent location to further examine the rural/urban differential in cancer incidence, particularly stage at diagnosis. A more complete understanding of the disparate cancer burden in Appalachia will help to generate hypotheses for future research and stimulate effective interventions leading to reductions in cancer mortality and improvements in cancer survival in this largely rural population.

References


