Cancer Surveillance Research

U.S. Geographic Distribution of Prevaccine Era Cervical Cancer Screening, Incidence, Stage, and Mortality

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Abstract

Background: Cervical cancer prevention programs are being reconfigured to incorporate human papillomavirus (HPV) testing and vaccination. To define priority areas for prevention efforts, we examined the geographic distribution of cervical cancer screening, incidence, stage, and mortality in the United States, prior to the introduction of HPV-based prevention technologies.

Methods: County-level cervical cancer incidence data from 37 central registries were obtained from Surveillance, Epidemiology, and End Results and North American Association of Central Cancer Registries. A spatial–temporal model that accounted for demographic and behavioral attributes was used to generate a complete view of county-level incidence from 1995 to 2004, including counties with missing data. Distribution of stage at diagnosis was examined by registry. Counties with high mortality and infrequent screening were identified using vital statistics and newly available county-level screening estimates.

Results: Compared with non-Hispanic whites and Asian and Pacific Islanders, incidence rates were higher among non-Hispanic black, American Indian and Alaska Native, and Hispanic women. Counties with infrequent screening often experienced elevated incidence and mortality rates and were located in states with suboptimal stage at diagnosis profiles. Affected areas included Appalachia, the southeastern Atlantic states, and the lower Mississippi Valley. Elevated death rates were experienced in central counties of large metropolitan areas.

Conclusions: Geographic and racial/ethnic variability were evident in cervical cancer incidence and mortality. Women living in areas with endemic poverty would benefit from access to HPV-based prevention technologies.

Impact: These findings provide a baseline for monitoring progress in cervical cancer control in the era of HPV-based prevention. *Cancer Epidemiol Biomarkers Prev; 20(4); 591–9. ©2011 AACR.*

Introduction

Before widespread screening and treatment of precancerous cervical lesions began in the late 1950s, cervical cancer was a leading cause of cancer death among American women (1). Although incidence and mortality rates have declined substantially during the last 50 years, 12,200 cervical cancer diagnoses and more than 4,200

deaths were estimated to have occurred among U.S. women in 2010 (2), with approximately 100,000 years of life lost in that year (3). In the United States, socioeconomic disparities are evident in of the burden of cervical cancer (4, 5). Recent reports confirm disparities in incidence (6, 7), mortality (8), and screening (9) across broad geographic regions. These geographic patterns and socioeconomic disparities suggest that cervical cancer screening should be more widely available and affordable.

Cervical cancer prevention programs face two major challenges: reducing cost and targeting women who are most likely to benefit from prevention efforts. Cervical cancer prevention is being revolutionized by the availability of 2 new technologies: human papillomavirus (HPV) testing and HPV vaccination (10). Including HPV testing in screening programs improves the sensitivity to detect invasive cervical cancer (11, 12), enabling screening programs to eliminate nearly all cervical cancers and reducing the number of screening visits for women who repeatedly test negative for HPV.

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Currently, approved HPV vaccines are effective against infections caused by HPV types 16 and 18, which cause about 70% of cervical cancers worldwide (13). However, the vaccines cannot clear HPV infections acquired prior to vaccination, and the cost of the vaccine is about $120 for each of 3 doses (14). The cost of vaccination and partial protection it provides led the World Health Organization to advise that HPV vaccines are one part of a coordinated cervical cancer prevention strategy, along with education and screening (15). As programs are reconfigured to incorporate HPV-based cervical cancer prevention technologies, accurate information will be needed to identify priority areas and populations for cervical cancer prevention.

This study provides the first comprehensive, nationally representative, and spatially explicit estimates of cervical cancer screening, incidence, and mortality. For the first time, estimates of cervical cancer incidence at the county level and by expanded racial groups are available for the entire United States. The results of spatial–temporal modeling presented here fill in gaps in high quality geographic cancer data. The nationwide maps of county-level estimates presented here allow visualization of regional patterns that could be obscured by administrative boundaries, such as state lines or census regions. These estimates provide a baseline against which to evaluate progress toward reducing cervical cancer incidence and mortality in the United States, following introduction of new prevention technologies.

Methods

County-level screening estimates

County-level estimates for 2000 to 2003 represent the predicted percent of adult women 18 years of age and older in the continental United States who reported having received a Papanicolaou test within the past 3 years. Small area estimates were obtained from a statistical methodology that utilizes responses from 2 national surveys (16, 17) and 27 county-level covariates from the 2000 Census (18) in a linear multivariate mixed model to generate small geographic area estimates for the continental United States (19, 20).

Incidence data

Incidence data from 1995 to 2004 were provided by Surveillance, Epidemiology, and End Results (SEER) and other North American Association of Central Cancer Registries (NAACCR) registries. A total of 37 registries met NAACCR gold or silver certification for high-quality incidence data and contributed county-level incidence data. NAACCR data standards specify quality control thresholds for the proportion of cases with missing age, race, stage, death certificate only cases, geocoding accuracy and completeness. Of 37 registries, 17 were missing 1 to 4 years of data. The model for estimating county-level incidence addressed partial and missing data. Data were accessed using SEER*Stat v.6.2.1 (IMS).

Incidence rates were estimated for 4 racial groups (non-Hispanic white, non-Hispanic black, Asian and Pacific Islander, American Indian and Alaska Native) and Hispanic ethnicity (all races). Fewer than 10,000 Hispanic women resided in North Dakota, South Dakota, Maine, or Vermont. Small populations of Asian and Pacific Islander women resided in these states and in West Virginia and Montana. To enhance the quality of racial classification for American Indians and Alaska Natives, case reporting was restricted to counties in Indian Health Service Contract Health Service Delivery Areas (CHSDA).

Stage at diagnosis

Stage at diagnosis for invasive cancer was reported by registries that contributed incidence data. Analysis was restricted to diagnosis years 2001 to 2003. "SEER Summary Stage 2000" categories: localized, regional, distant, and unstaged were used in analysis (21).

Mortality data

County-level cervical cancer mortality rates from the National Center for Health Statistics were age adjusted to the 2000 U.S. Standard Population. SEER*Stat (IMS) was used to assess cervical cancer mortality by race and ethnicity in the 5 most densely populated metropolitan areas in the United States: Los Angeles County, the Boroughs of New York, Cook County (Chicago), Harris County (Houston), and Philadelphia County.

Statistical analysis

Predicted county-level incidence

A spatial and temporal model was used to estimate incidence rates for all U.S. counties by race and ethnicity. The model (22, 23) is based on associations between observed incidence and mortality within SEER and NAACCR registries and sociodemographic and lifestyle factors at the county level. Three of 27 county-level covariates in the model had missing data (<0.3% missing): percent of people meeting exercise guidelines, adult women who ever smoked, and adult women who had a Pap smear within 5 years. Missing county-level responses were replaced with state-level estimates. Validation studies (24) show that the model provides accurate estimates of case counts.

The models incorporated county-level covariates from multiple sources. These included NAACCR and SEER incidence cases stratified by race and Hispanic ethnicity, 10 age groups (0–4, 5–14, 15–24, 25–34, . . ., 85+), county of residence, and year of diagnosis; U.S. 2000 Census sociodemographic attributes including age distribution, racial and ethnic population composition, income, poverty, education, household characteristics (18), and county-level rural–urban continuum scores (25). The model incorporated county-level data about the availability of physicians, cancer screening facilities, and health insurance (26). Additional inputs included tobacco use, obesity, and cervical cancer screening rates from the

Behavioral Risk Factor Surveillance System (18). Cervical cancer mortality inputs were stratified by 10 age groups, race, county, and year of death. In Alaska, covariates were applied at the state level. Incidence and mortality counts for Alaska were classified by 3 regions—Anchorage Municipality, Fairbanks North Star Borough, and remaining areas. Inputs for Hispanic ethnicity were restricted to states with reliable data on whether or not cases were Hispanic. Mortality data for Hispanic ethnicity was restricted to states and years, according to the Hispanic index criterion (27). Thus, cancer deaths for non-Hispanic whites, non-Hispanic blacks, and Hispanics in the following states and years were excluded: Maine (1995–1998), Minnesota (2002), New Hampshire (1995–2000, 2003), North Dakota (1995–1996, 1998–2004), and Oklahoma (1995–1996).

Predicted incidence rates were age adjusted using the 10 age groups in the model, then delay adjusted using adjustment factors specific to cervical cancer and diagnosis year. Delay adjustment accounted for underreporting of cancer rates due to delays in case reporting by registries (28). The 1995 to 2004 delay adjustment factors by race, age, and year of diagnosis for cervical cancer ranged from 0.73% to 4.0%.

Mapping

Uncertainty related to small numbers of cases in low-population counties was addressed by spatial smoothing. Geographic smoothing algorithms borrow information from neighboring area to stabilize results from sparsely populated areas. A nonparametric algorithm used population weights to smooth underlying variation, while retaining broad patterns in the data (29). Model-based county-level screening rates were mapped without spatial smoothing. Age- and delay-adjusted county-level incidence rates (model based) and age-adjusted mortality rates (observed) were smoothed using the head-bang algorithm with established model parameters (ref. 29; HeadBang plug-in for ESRI ArcMap v.3.0; NCI).

Screening rates were mapped in quartile intervals. After incidence and mortality rates were smoothed, data were mapped in quintile intervals (ESRI ArcMap 9.3). Geographic patterns refer to the Census Bureau Regions and Divisions. Incidence rate maps were not presented for American Indians and Alaska Natives due to small case counts in CHSDA counties. Instead, rates are described by Indian Health Services regions: Northern Plains, Southern Plains, Alaska, Pacific Coast, and East.

Results

Screening rates

Areas identified as having low usage of traditional cervical cancer screening methods included regions of Appalachia (from the southern tier of New York to northern Alabama, Mississippi, and Georgia), the central Mississippi Valley (including Missouri, Kentucky, and Tennessee), West North Central states (spanning North and South Dakota, Nebraska), Texas, Florida, and the lower Mountain states of Arizona, New Mexico, and Utah (Fig. 1).

Overall incidence and mortality rates

Cervical cancer incidence and mortality rates for women of all races and ages from 1995 to 2004 are presented in smoothed county-level maps (Fig. 2). Among the locations with the highest estimated incidence rates were areas of Appalachia, the South Atlantic,

Figure 1. Percent of women ages 18 years and more who reported having had a Papanicolaou smear test within the past 3 years by county—continental United States, 2000 to 2003. Modeled estimates based on Behavioral Risk Factor Surveillance System, National Health Interview Survey, and county-level census data.
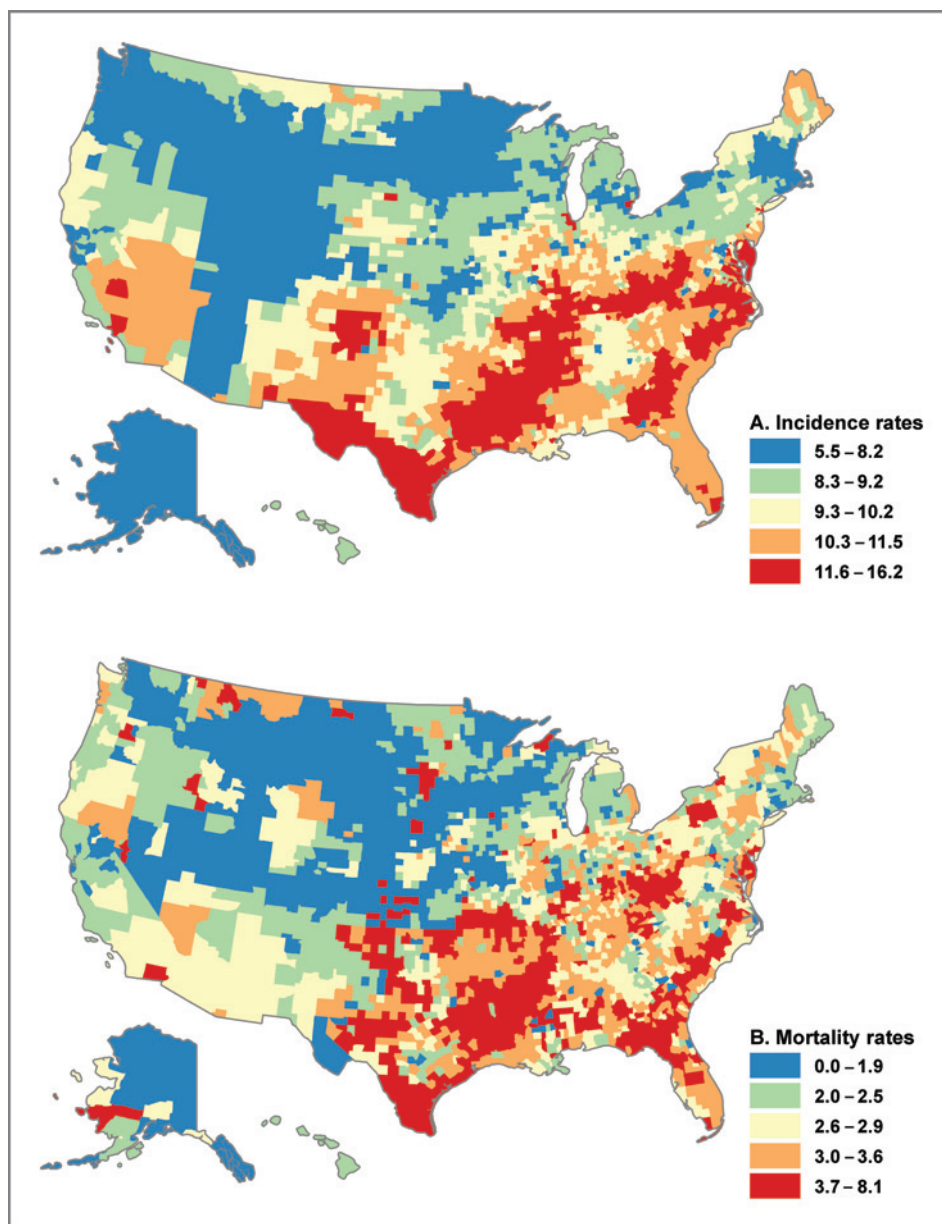
Percent screened in past 3 years
- 80.9% – 90.5%
- 79.1% – 80.8%
- 77.4% – 79.0%
- 69.8% – 77.3%
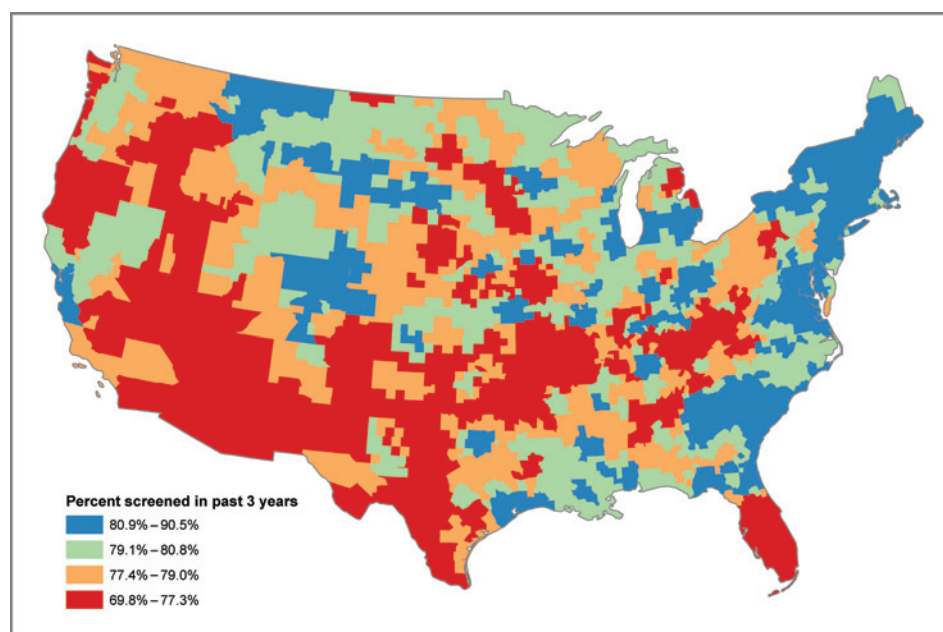
Figure 2. Predicted U.S. cervical cancer incidence (A) and mortality rates (B) by county, 1995 to 2004.

the lower Mississippi Valley, along the Texas–Mexico border, and the region of the Oklahoma and Texas Panhandles. Cervical cancer mortality rates followed similar geographic patterns, with additional elevated death rates observed in small areas such as parts of the West North Central and Mountain regions.

Racial and ethnic incidence rates

The overall estimated delay- and age-adjusted incidence rate (all rates per 100,000 women) for the United States from 1995 through 2004 was 9.7. Estimated rates were elevated in some racial-ethnic groups (e.g., 15.3 among Hispanics, and 14.4 among non-Hispanic blacks). The estimated incidence rate among American Indian

and Alaska Native women (9.9) was only slightly higher than the overall United States incidence rate. Incidence rates were lower than the national rate among both Asian and Pacific Islander women (9.1) and non-Hispanic white women (8.5).

The geographic distribution of counties with elevated cervical cancer incidence rates among non-Hispanic white women and non-Hispanic black women was similar visually to the overall pattern for U.S. women (Fig. 3). Additional areas with elevated incidence rates among Asian and Pacific Islander women and Hispanic women included in the West South Central and West North Central regions. Estimated county-level incidence rates among non-Hispanic black and Hispanic women had
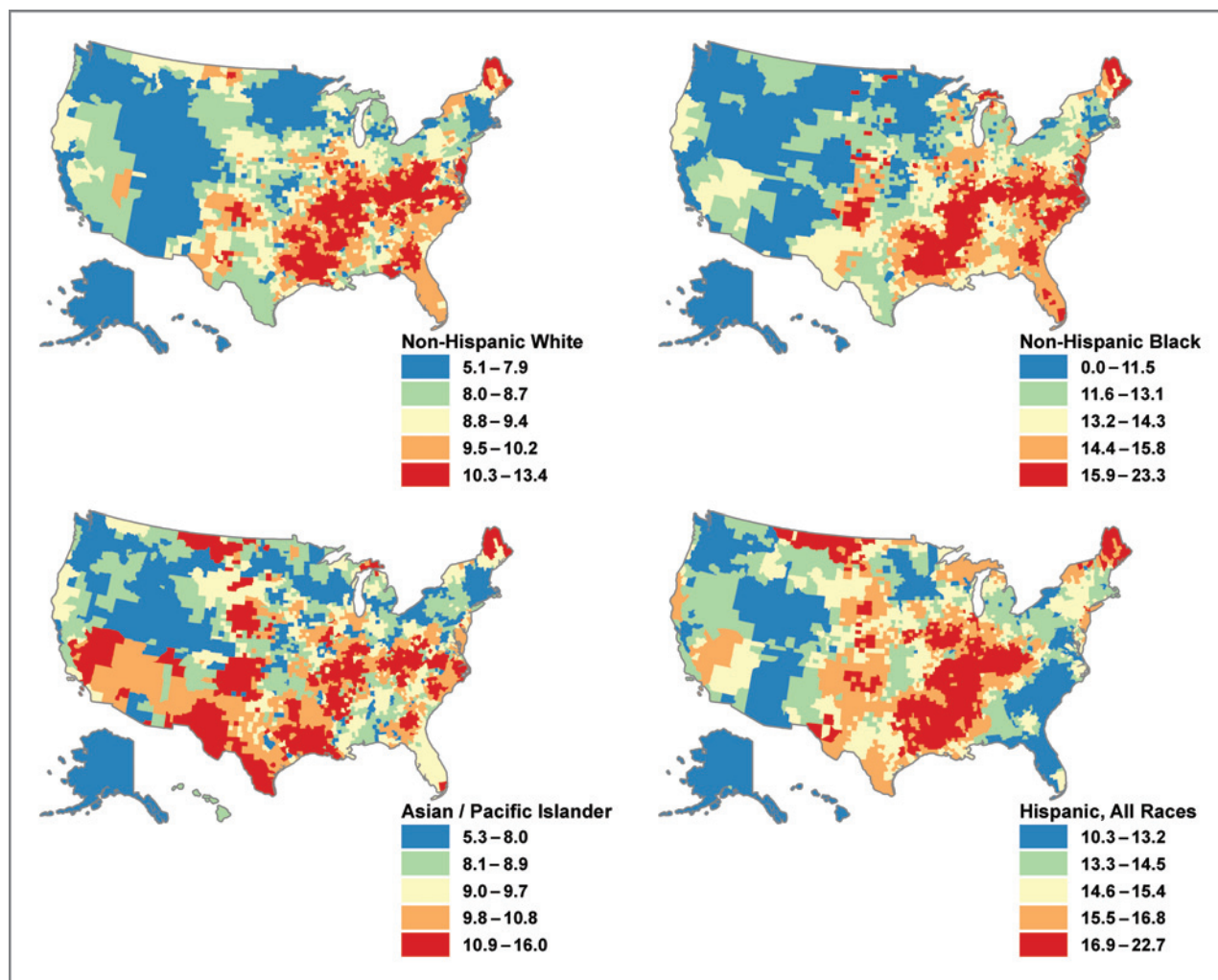
Figure 3. Geographic distributions of estimated U.S. cervical cancer incidence rates among racial and ethnic groups by county, 1995 to 2004.

higher maximum values (~23 per 100,000) than those of non-Hispanic white (13.4) and Asian and Pacific Islander women (16.0).

Estimated incidence rates among American Indian and Alaska Native women were highest in the Southern and Northern Plains (15.3 and 10.6 per 100,000, respectively), followed by the Eastern United States (10.2). The estimated rate in Alaska was 8.7, with lower incidence rates in the Southwest and Pacific Coast: 7.5 and 6.9, respectively.

Stage at diagnosis

Stage at diagnosis data from 2001 through 2003 for participating registries were sorted in descending order of favorability on the basis of the percent of cases diagnosed at localized stage and the percent with known stage (Table 1). In 8 registries with the best stage at diagnosis profiles—Rhode Island, Hawaii, Utah, Oregon, Maine, South Carolina, Washington, and Massachusetts—at least 55% of cases were diagnosed at localized stage. These same registries also had less than the 7% average proportion of cases with missing stage information. In 17 registries, at least 50% of cases were diagnosed with localized stage cancer or had less than 7% with missing stage. In the remaining 12 registries, at least 7% of cases had missing stage and, except for Ohio and West Virginia, less than half of the cases were diagnosed with localized stage cancer.

Mortality rates in urban counties

In central counties of the five largest urban areas in the United States (Table 2), mortality rates exceeded 3.0 deaths per 100,000 person-years, with a rate of 4.5 per 100,000 in Philadelphia County. Among racial-ethnic groups, Hispanic women accounted for the highest number of deaths in Los Angeles County. Non-Hispanic black women had the highest death counts in New York, Cook, and Philadelphia County. Non-Hispanic white women accounted for the largest fraction of deaths in Harris County.

Table 1. Stage at diagnosis, invasive cervical cancer cases, 37 registries, 2001 to 2003

Registry	Stage at Diagnosis (%)			
	Localized	Regional	Distant	Missing
Rhode Island	68	25	8	5
Hawaii	62	25	12	1
Utah	57	33	10	2
Oregon	55	37	8	3
Maine	59	37	4	7
South Carolina	59	35	6	7
Washington	55	36	9	4
Massachusetts	55	37	8	4
Missouri	51	38	11	3
Louisiana	52	39	10	5
Nebraska	50	40	10	4
California	49	39	12	4
Alaska	55	41	5	9
Nevada	54	38	7	9
Colorado	54	38	8	9
Georgia	50	41	9	6
Idaho	52	39	9	8
New Mexico	51	40	10	7
Pennsylvania	51	39	10	7
Wisconsin	55	40	6	11
Alabama	49	41	10	6
Illinois	50	40	10	7
Indiana	49	42	8	7
New Hampshire	49	42	10	7
Connecticut	46	42	13	5
Kentucky	49	41	10	8
Iowa	47	39	14	7
Ohio	51	41	8	12
Montana	46	50	5	8
New Jersey	45	44	11	8
Michigan	49	41	10	13
West Virginia	50	40	9	16
Texas	48	44	8	15
Florida	45	46	9	14
Arizona	45	47	8	18
New York	43	48	9	17
Washington DC	36	57	7	32

NOTE: Based on SEER Summary Stage 2000.

Discussion

This study provides a pre-HPV vaccine baseline of the burden of cervical cancer and uptake of screening in the United States. Despite the knowledge and technology to prevent and treat this disease, significant numbers of women continue to be diagnosed with and die as a result of cervical cancer (30). Disparities were evident in specific geographic areas and demographic subgroups.

The racial-ethnic incidence maps in this study reflect persistent cervical cancer disparities (6). Women of His-panic ethnicity, non-Hispanic black women, and American Indian and Alaska Native women experienced a higher burden of cervical cancer incidence compared with non-Hispanic white and Asian and Pacific Islander women. Our findings are also consistent with studies, suggesting that women in socioeconomically deprived areas are among those who experience the highest rates of cervical cancer in the nation (7, 8, 31).

Counties with low screening rates often overlapped with areas of elevated incidence and mortality rates, such as in the counties along the Texas–Mexico border, or were

Table 2. Cervical cancer mortality rates and counts in urban centers of the 5 largest metropolitan areas in the United States, 2002 to 2006, by race[a]

| Metropolitan Area, State | All Races[b] | | Non-Hispanic | | | | | | | |
| | | | White | | Black | | Asian/Pacific Islander | | Hispanic, All Races | |
	Rate (95% CI)	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count
Los Angeles County, CA	3.1 (2.9–3.4)	753	2.4	232	4.0	96	2.7	99	4.3	323
New York City, NY	3.1 (2.9–3.4)	722	2.1	210	6.9	285	2.2	46	3.6	173
Cook County, IL	3.3 (3.0–3.6)	470	2.2	180	6.3	225	1.5	10	2.9	51
Harris County, TX	3.4 (3.0–3.8)	278	2.4	105	5.6	80	3.1	11	4.6	82
Philadelphia County, PA	4.5 (3.8–5.2)	183	2.9	60	6.2	110	—[c]	—[c]	—[c]	—[c]

[a]Age-adjusted rates per 100,000 women for the years from 2002 through 2006.
[b]All races includes women of Hispanic and non-Hispanic ethnicity. Asian and Pacific Islander not exclusive of Hispanic ethnicity.
[c]Data suppressed in 2 groups when less than 10 deaths occurred in one cell (—).

located in states with less than favorable stage at diagnosis profiles, such as Kentucky and West Virginia. Stage at diagnosis patterns were consistent with those of a study that examined disparities in Appalachia, in which the authors suggested that the high proportion of unstaged cancer may relate to limited access to health care (31). Reminiscent of a study of rural–urban cancer stage disparities in Illinois (32), elevated cervical death rates were experienced in the 5 most densely populated counties in the United States. Urban disparities in cervical cancer mortality in Philadelphia, Houston, Chicago, Los Angeles, and New York suggest a need for city center–based cervical cancer prevention programs.

Multiple factors contribute to the differential utilization of preventive and treatment services that underlie the disparities and geographic patterns described here. At the system level, these factors include lack of health insurance, lack of nearby health care facilities, and underfunding of facilities that service high-risk areas. Factors at the provider level include failure to consistently recommend appropriate screening or follow-up care, or to monitor compliance with recommendations in settings that service disadvantaged women. Underserved women also face individual barriers, including lack of transportation or childcare to facilitate provider visits, an insufficient knowledge base to ensure compliance, language, and acculturation barriers to navigating the health care system, and cultural beliefs and attitudes that limit health care seeking behavior. Improvements in access to care resulting from tailored interventions that address the specific socioeconomic and cultural issues facing high-risk communities may address these issues (33). Importantly, community organizations and trained local advocates play a significant role in increasing utilization of cancer control services by underserved women.

Cancer control planners may use these maps to identify urban and rural areas within their state with low screening uptake, high incidence, or mortality rates and target interventions accordingly (*Steps to Effective Cancer Control Planning*, http://cancercontrolplanet.cancer.gov). The maps may also be used to define at-risk racial and ethnic populations within affected areas for timely vaccination or screening and follow-up services. Local coalitions could use such findings to more effectively target health services and culturally sensitive approaches to reach at-risk populations.

With the onset of HPV testing and prophylactic vaccination, recent studies highlight progress in adoption of HPV-based preventive services among high-risk populations. The Advisory Committee on Immunization Practices recommends that the newly licensed quadrivalent HPV vaccine be administered among girls (34). In 2008, racial and socioeconomic variation in uptake of the HPV vaccine suggested that at least the initial dose was reaching appropriate population targets (35). Specifically, uptake of at least 1 dose of vaccine was 44% among Hispanics, 36% among blacks, 35% among whites, and 46% among girls below the poverty level compared with 36% among girls at or above the poverty level. State-level variation in vaccine uptake, however raises questions of whether coverage is aligned optimally with risk. In 2008, for example, the state with the highest rate of HPV vaccine coverage was Rhode Island whereas Mississippi had the lowest rate of HPV vaccine coverage, despite having twice the cervical cancer mortality rate of Rhode Island (36).

Caution is warranted against overinterpretation of county-level rates. Smoothing of county incidence rates could mask geographic variation in areas with few cases. Hispanic ethnicity is often underreported on hospital records and death certificates (37, 38), and certain years used in the analysis have restricted information on Hispanic ethnicity. Despite limitations, this report provides a useful geographic baseline of cervical cancer screening,

incidence, stage, and mortality in the United States before the introduction of HPV-based screening technologies and vaccines.

The priorities of the next generation of HPV-based cervical cancer prevention programs include reducing cervical cancer incidence and mortality in high-risk areas and populations such as those identified in this study and reducing costs and adverse events associated with screening in areas with low incidence or high use of screening techniques (10). Although HPV vaccination may seem to be an attractive option in high-risk areas and populations, the vaccine is expensive. Without school vaccination mandates, HPV vaccine uptake among girls ages 13 to 17 in 2008 was only 37.2% for the first dose and 18% for the full series (35). Furthermore, the approved vaccines prevent only about 70% of cervical cancer, and the benefit will take decades to be realized because vaccination does not clear preexisting HPV infection (13). Although screening programs incur costs and require medical infrastructure, screening immediately benefits women with current persistent HPV infections (39). With HPV-based testing (13), screening programs will be more sensitive and require fewer visits (10). With effective implementation (40), a combination of HPV vaccination and reduced frequency HPV-based screening could manifest the best of both modes of prevention with minimal drawbacks.

Results of this study show the value of spatially explicit estimates for identifying regions of the country that could benefit most from targeted allocation of cancer control resources and/or more effective interventions that are tailored to the needs of high-risk populations. As targeted approaches to cancer control in high-risk areas are adopted in the era of HPV-based screening and prophylactic vaccination, population-based surveillance research that includes small area estimation and mapping must continue to play a critical role in monitoring their effectiveness. In the future, progress toward reducing incidence and mortality may be evaluated against the baseline data presented in this study.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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