Cancers With Increasing Incidence Trends in the United States: 1999 Through 2008

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Abstract

Despite declines in incidence rates for the most common cancers, the incidence of several cancers has increased in the past decade, including cancers of the pancreas, liver, thyroid, and kidney and melanoma of the skin, as well as esophageal adenocarcinoma and certain subsites of oropharyngeal cancer associated with human papillomavirus (HPV) infection. Population-based incidence data compiled by the North American Association of Central Cancer Registries were used to examine trends in incidence rates from 1999 through 2008 for the 7 cancers listed by sex, age group, race/ethnicity, and stage at diagnosis. Joinpoint regression was used to calculate average annual percent changes in incidence rates (1999-2008). Rates for HPV-related oropharyngeal cancer, esophageal adenocarcinoma, cancer of the pancreas, and melanoma of the skin increased only in whites, except for esophageal adenocarcinoma, which also increased in Hispanic men. Liver cancer rates increased in white, black, and Hispanic men and in black women only. In contrast, incidence rates for thyroid and kidney cancers increased in all racial/ethnic groups, except American Indian/Alaska Native men. Increases in incidence rates by age were steepest for liver and HPV-related oropharyngeal cancers among those aged 54 to 64 years and for melanoma of the skin in those aged 65 years and older. Notably, for HPV-related oropharyngeal cancer in men and thyroid cancer in women, incidence rates were higher in those aged 55 to 64 years than in those aged 65 years and older. Rates increased for both local and advanced stage diseases for most cancer sites. The reasons for these increasing trends are not entirely known. Part of the increase (for esophageal adenocarcinoma and cancers of the pancreas, liver, and kidney) may be linked to the increasing prevalence of obesity as well as increases in early detection practices for some cancers. These rising trends will exacerbate the growing cancer burden associated with population expansion and aging. Additional research is needed to determine the underlying reasons for these increasing trends. CA Cancer J Clin 2012;62:118-128. ©2012 American Cancer Society.

Introduction

Overall, incidence rates are decreasing in the United States for most cancer sites, including lung, colon and rectum, prostate, stomach, and cervical cancers, in part due to reductions in smoking prevalence (lung), increased screening and removal of premalignant lesions (colon and cervix), improved hygiene (stomach), and changes in the use of prostate-specific antigen testing. In contrast, rates are increasing for several major cancer sites and subtypes, including human papillomavirus (HPV)-related oropharyngeal cancer; esophageal adenocarcinoma; cancer of the pancreas, liver and intrahepatic bile duct, thyroid, and kidney and renal pelvis; and melanoma of the skin. As a result, the public health importance of these cancers will rise as they increasingly contribute to the overall cancer burden. In this article, we provide incidence rates and trends, and 5-year relative survival rates, by demographic characteristics, to increase awareness in the clinical community and to spur additional research into the causes of these observed increases.
Materials and Methods

Incidence data for calculating cross-sectional rates (2004-2008) and for analyzing long-term trends (1999-2008) by sex, race/ethnicity, and age were obtained from the North American Association of Central Cancer Registries (NAACCR), a compilation of population-based cancer registries that includes data from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program and the Centers for Disease Control and Prevention National Program of Cancer Registries. Forty-eight states contributed to the cross-sectional rate analyses and 41 states to the long-term trend analyses, covering 96% and 86% of the US population, respectively. Analyses of incidence trends by stage at cancer diagnosis and relative survival rates were based on 13 SEER areas covering 14% of the US population. Table 1 lists the names of the registries included in each of these analyses. The race/ethnicity, age, and stage at diagnosis categories used in these analyses were the 5 major racial and ethnic groups (white, black, Asian or Pacific Islander, American Indian or Alaska Native [restricted to Contract Health Service Delivery Areas], and Hispanic ethnicity of any race), 3 broad age groups (ages 15-54 years, ages 55-64 years, and aged 65 years and older), and SEER historic stage A (stage at cancer diagnosis was classified as local, regional, distant, and unknown). 4

The 7 cancers evaluated were selected for inclusion in the current study based on the observation that their overall incidence rates were generally increasing over time for both men and women during 1999 through 2008. Invasive cancer cases were coded by site and/or histology according to the third edition of the International Classification of Diseases for Oncology (ICD-O-3). The histology codes for esophageal adenocarcinoma in ICD-O-3 were 8140 to 8575. Cases of HPV-associated oropharyngeal cancers were selected with ICD-O-3 topography codes for base of the tongue (C019), lingual tonsil (C024), palatine tonsil (C090-099), oropharynx (C100-109), and Waldeyer ring (C14.2), restricted to squamous cell histologies (ICD-O-3 codes 8050-8084). As many as 60% of malignancies in these subsites are associated with HPV infection. By race and ethnicity, during 1999 through 2008, incidence rates of HPV-related oropharyngeal cancers increased by 4.4% per year among white men and by 1.9% per year among white women, and there were no significant differences in incidence rates among men and women of other racial and ethnic groups (Table 2). In persons of all races and ethnicities combined, incidence rates increased among men in all age groups and among women for using joinpoint regression, which involves fitting a series of joined straight lines on a logarithmic scale to the trends in annual age-standardized rates. A maximum of one joinpoint was allowed in the model for the period 1999 through 2008 and trends in incidence are reflected by the average annual percent change (AAPC), a weighted average of the annual percent change calculated by the model over time. Significance of the AAPCs was assessed using a 2-sided Z-test, and P values < .05 were considered significant. All rates presented were age standardized to the 2000 US standard population and expressed as per 100,000 population. The 5-year relative survival rates (expressed as a percentage) by anatomic site and stage at diagnosis were calculated for the following time periods: 1992 through 1995, 1996 through 1999, and 2000 through 2007, among those with cancers diagnosed between January 1992 and December 2007, and followed through December 2008. Relative survival reflects the likelihood of surviving 5 years after cancer diagnosis, and is the ratio of the observed survival in people with cancer to the expected survival in the general population with the same distribution of age, sex, and race obtained from standard life tables.

Selected Findings By Cancer Site

HPV-Related Oropharyngeal Cancer

The overall incidence of oropharyngeal cancers has been declining for some time in the United States, and incidence rates peaked in the early 1980s for both black and white men. However, in 2000, an increase in incidence rates among white men was observed, and at about the same time, evidence of HPV DNA was detected in samples from oropharyngeal tumors. Further studies identified HPV infection as a major risk factor for cancers at these subsites and as many as 60% of these tumors are associated with HPV infection. By race and ethnicity, during 1999 through 2008, incidence rates of HPV-related oropharyngeal cancers increased by 4.4% per year among white men and by 1.9% per year among white women, and there were no significant differences among men and women of other racial and ethnic groups (Table 2). In persons of all races and ethnicities combined, incidence rates increased among men in all age groups and among women for
those ages 15 to 54 years and 55 to 64 years (Fig. 1). By stage at diagnosis, rates increased for regional and distant staged tumors (Fig. 2). The increasing incidence rates for HPV-related oropharyngeal cancers are in stark contrast to steady declines in rates for HPV-unrelated oropharyngeal cancers, largely due to decreases in smoking prevalence.\(^{14}\) Reasons for these increasing rates are unclear, but changing sexual practices (including oral-genital sexual contact) are hypothesized to be important.\(^{9,13,15}\) The most dramatic increase in rates was among men ages 55 to 64 years, which is consistent with changes in HPV exposure patterns for men born after the mid-1940s.\(^{7}\)

Existing data do not provide a clear explanation for the observed differences by race in incidence trends for HPV-related oropharyngeal cancer. One clinical study of patients with American Joint Committee on Cancer stages III and IV squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, and larynx found that blacks were much less likely than whites to have HPV type 16 (HPV16)-positive tumors, and it was hypothesized that this difference might be related to a higher prevalence of oral-genital contact in white compared with black adolescents.\(^{16,17}\) However, our analysis found identical incidence rates for HPV-related cancer (8.0 per 100,000) among white and black males, with HPV-related subsites representing 42% of all oropharyngeal cancers in white men and 43% in black men. In addition, a study of risk factors for oral HPV infection found no evidence of an association with self-reported oral sex, but did find evidence suggestive of an association between oral HPV infection and increasing number of lifetime sexual partners as well as tobacco smoking.\(^{18}\)

Although the pathway by which HPV induces the malignant transformation of oropharyngeal cells is unclear, it may be similar to that involving HPV-related cervical cancer, where persistent infection is a critical component.\(^{19}\) Additional research is needed to clarify the routes of oral HPV transmission and to determine the natural history of HPV infection in the oral cavity and oropharynx, along with related genetic instability in the malignant transformation of cells, and to develop appropriate prevention strategies. Furthermore, increased awareness among clinicians may also aid in the detection of early stage lesions. While HPV vaccination has been shown to prevent cervical cancer among women,\(^{20,21}\) and genital warts and anal cancer among men and women,\(^{22}\) data are lacking to demonstrate the potential efficacy of vaccination in preventing HPV-associated malignant conditions in the oral cavity and oropharynx, underscoring the need for additional studies in these areas.

Esophageal Adenocarcinoma

Incidence rates for adenocarcinoma of the esophagus have been increasing for decades in the United States, in sharp contrast to declining trends for squamous cell carcinoma of the esophagus.\(^{23}\) From 1999 to 2008, incidence rates for esophageal adenocarcinoma increased significantly among white men

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**TABLE 1. Population-Based Cancer Registries Included in the Current Analyses**

| Cross-sectional rates presented for 2004 through 2008 (48 states) |
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| Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming. |

| Long-term trends in rates for 1999 through 2008 (41 states) |
|---|
| Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nebraska, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Texas, Utah, Vermont, Washington, West Virginia, Wisconsin, and Wyoming. |

| Five-year relative survival rates from 13 SEER areas |
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| California (Los Angeles, San Francisco-Oakland, and San Jose-Monterey), Connecticut, Georgia (Metropolitan Atlanta and rural Georgia), Hawaii, Iowa, Michigan (Detroit), New Mexico, Washington (Seattle Puget Sound), Utah, and Alaska Native Registry. |

SEER indicates Surveillance, Epidemiology, and End Results.
(1.8% per year), white women (2.1% per year), and Hispanic men (2.8% per year), while there were no significant changes observed for men or women of other racial/ethnic groups (Table 2). By age, rates increased for men and women aged 55 years or older (Fig. 1) and by stage at diagnosis for distant and regional staged disease (Fig. 2). Obesity is an established risk factor for esophageal adenocarcinoma, as is gastroesophageal reflux disease, through the establishment of Barrett esophagus (a premalignant condition that can progress to esophageal adenocarcinoma).

These increasing trends in incidence rates of esophageal adenocarcinoma coincide with rises in obesity and gastroesophageal reflux disease prevalence, although it is believed that these factors do not wholly explain the observed trends in rates.

Incidence rates of esophageal adenocarcinoma were 7-fold higher among white versus black men, although the causes of these differences are unclear (Table 2). Paradoxically, overall obesity prevalence is higher among black men and women than among white men and women, although rates of...
esophageal adenocarcinoma are only increasing among white men and women and Hispanic men. These trends may be reflective of the prevalence of abdominal (central) obesity, which is associated with an increased risk of gastroesophageal reflux and Barrett esophagus, and is higher among white men and women relative to black men and women.\textsuperscript{29} Although the precise mechanism is not clearly understood, \textit{Helicobacter pylori (H. pylori)} infection is associated with a reduced risk of adenocarcinoma of the esophagus,\textsuperscript{30} and the lower prevalence of \textit{H. pylori} infection among whites may also contribute to racial differences in esophageal adenocarcinoma risk.\textsuperscript{23} The pathways by which these factors influence esophageal carcinogenesis, and possibly interact, should be clarified with additional research.\textsuperscript{24–26}

\textbf{FIGURE 1. Cancers With Increasing Incidence Rates by Anatomic Site, Sex, and Age Group, 1999 Through 2008.} HPV indicates human papillomavirus. Rates are age adjusted to the 2000 US standard population. Note the scale of the Y axis differs between cancer sites and sex. HPV-related oropharynx is restricted to squamous cell histologies for cancers of the base of the tongue, lingual tonsil, palatine tonsil, oropharynx, and Waldeyer ring. Source: Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: NAACCR Incidence-CiNA Analytic File, 1995-2008, for Expanded Races, Custom File With County, ACS Facts & Figures Projection Project, North American Association of Central Cancer Registries. Bethesda MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program, Cancer Statistics Branch; 2011.
Five-year relative survival rates for esophageal adenocarcinoma increased somewhat over time, although survival remained poor for distant staged tumors (2.9% during 2000-2007) (Table 3).

Maintaining a healthy body weight may be an important prevention strategy for esophageal adenocarcinoma. The treatment of patients with gastroesophageal reflux disease with proton-pump inhibitors, which reduces gastric acid thereby slowing or precluding the development of Barrett esophagus, may also be considered, although the most effective regimen to reduce cancer risk is not known.23 In addition, medical surveillance for the development of esophageal adenocarcinoma among

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**Table 3. Five-Year Relative Survival Rates for Cancers With Increasing Incidence in the United States by Anatomic Site, Stage, and Calendar Period at Diagnosis**

| ANATOMIC SITE AND CALENDAR PERIOD | LOCALIZED, % | REGIONAL, % | DISTANT, % |
|----------------------------------|-------------|-------------|-----------|
| HPV-related oropharynx           | 63.3        | 67.0        | 76.7      |
| Esophageal adenocarcinoma        | 33.5        | 37.7        | 47.8      |
| Pancreas                         | 15.5        | 15.3        | 21.3      |
| Liver and intrahepatic bile duct | 12.5        | 19.3        | 26.9      |
| Thyroid                          | 99.4        | 99.5        | 99.8      |
| Kidney and renal pelvis          | 88.4        | 88.7        | 91.1      |
| Melanoma of the skin             | 96.1        | 98.3        | 99.3      |

HPV indicates human papillomavirus. Analyses were restricted to persons aged older than 15 years. Five-year relative survival was calculated using the actuarial method and is expressed as percentages during 1992 through 2007 according to Surveillance, Epidemiology, and End Results (SEER) historic stage.

Source: Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: Incidence-SEER 17 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov. 2010 Sub (1973-2008 varying). Bethesda, MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program, Cancer Statistics Branch; 2011. Released April 2011 based on the November 2010 submission.
those with Barrett esophagus may also be beneficial, although the optimal screening interval is unknown.31

Pancreas

Increases in pancreatic cancer incidence rates were limited to white men (0.9% per year) and white women (1.0% per year) during 1999 through 2008 (Table 2). Incidence rates also increased for men aged 55 years or older and for women of all ages (Fig. 1) as well as for local, regional, and distant staged tumors (Fig. 2). Tobacco use (which has been declining in recent decades) and obesity (which has been increasing over time) are established risk factors; however, the causes of the observed increases in pancreatic cancer incidence rates are not known.32,33 While the prevalence of adult obesity is higher among blacks compared with whites, the isolated increases observed among whites suggests the presence of other factors resulting in increasing pancreatic cancer rates among white men and women.28

During 2004 through 2008, pancreatic cancer incidence rates (per 100,000 population) were highest among black men (21.3) and women (17.6) relative to white men (16.8) and women (12.8). The racial disparity in the burden of pancreatic cancer has been explained in part by increased cigarette smoking and diabetes mellitus among black men versus white men, and heavy alcohol consumption and elevated body mass index among black women versus white women.34

Five-year survival for pancreatic cancer was poor regardless of disease stage, and did not improve over time (Table 3). During 2000 through 2007, the 5-year survival rates were 21.3% for local stage cancer, 8.9% for regional stage cancer, and 1.8% for distant stage cancer.

Avoiding tobacco use and maintaining a healthy body weight are important prevention measures for cancer of the pancreas. While no screening procedures are currently recommended at the population level, those with extremely high risks for pancreatic cancer (eg, individuals with genetic mutations associated with pancreatic cancer and/or a strong family history) may benefit from endoscopic ultrasonography or screening for the molecular markers associated with pancreatic cancer.35

Liver and Intrahepatic Bile Duct

Significant increases in liver cancer incidence rates were observed among white (3.8% per year), black (5.4% per year), and Hispanic men (2.4% per year) and among black women only (2.7% per year) during 1999 through 2008 (Table 2). Incidence rates increased for all age groups, most notably for men ages 55 to 64 years (Fig. 1). Liver cancer incidence rates increased for all stages at diagnosis, although most notably for localized disease: from 2.3 in 1999 to 4.2 in 2008 (Fig. 2). Chronic hepatitis C virus (HCV) infection is a cause of liver cancer, and the increasing burden of liver cancer among black men and women, especially those aged 55 to 64 years, is consistent with an aging cohort of people infected with HCV in the past who are now reaching ages at which liver cancer risk is highest.36 Other important causes of liver cancer in the United States are excessive alcohol consumption leading to alcoholic cirrhosis, which has been declining, and obesity, which has been increasing.37

Five-year relative survival rates for localized liver cancer increased from 12.5% during 1992 through 1995 to 26.9% during 2000 through 2007 (Table 3). These trends may reflect the impact of surveillance among high-risk groups, and improved outcomes associated with transplantation and resection of early stage tumors.38 There was little improvement in 5-year survival for regional or distant staged cancers.

Despite increasing trends in white, black, and Hispanic men and black women, liver cancer rates (per 100,000 population) continue to be highest among Asian or Pacific Islander men (27.6) and women (10.4) (Table 2). Chronic hepatitis B virus (HBV) infection is a risk factor for liver cancer, and the high incidence rates noted among Asians and Pacific Islanders reflect the substantial burden of endemic HBV infection among those born elsewhere who emigrated to the United States.39,40 The increasing incidence trends and high burden of disease in differing population subgroups warrant continued monitoring as rates may continue to rise.

Hepatitis B vaccination prevents HBV-related liver cancer, and is recommended for newborns and high-risk adults.31,42 Transmission of HBV and HCV may also be stymied through safe injection drug practices and proper and consistent condom use. In addition, antiviral treatment of chronic HBV
or HCV infections also reduces liver cancer risk. Avoiding tobacco use and limiting alcohol consumption are also important prevention measures, as is maintaining a healthy body weight. Persons at high risk for liver cancer (eg, those with HBV-related or HCV-related cirrhosis) may be screened every 6 months via ultrasound, although the effectiveness of such screening is unclear.

**Thyroid**

In contrast to the observed trends for HPV-related oropharyngeal cancer, esophageal adenocarcinoma, and pancreatic cancer, where increases were largely restricted to white men and women, thyroid cancer incidence rates significantly increased among men and women of every racial/ethnic background (except American Indian or Alaska Native men) during 1999 through 2008 (Table 2). Rates increased for men and women of all ages, most notably for women ages 55 to 64 years (Fig. 1). Incidence rates increased for tumors of all stages, although the greatest increase was in the incidence of localized disease (from 5.2 in 1999 to 9.6 in 2008) (Fig. 2). Reasons for the rising incidence rates of thyroid cancer are not known. Some studies have suggested the increasing rates may be due to the enhanced medical scrutiny of small tumors that may have otherwise gone undiagnosed (detected through ultrasound and confirmed via fine-needle aspiration); however, a series of recent analyses found increases in thyroid cancer incidence rates across sex and racial/ethnic groups, as well as increases in incidence by tumor size (both small and large tumors). These consistent increases across multiple categories suggest that enhanced detection cannot be the sole factor driving the observed trend. The major known exogenous risk factor for thyroid cancer is radiation exposure during childhood (eg, through medical treatments during childhood or through fallout from nuclear accidents). In addition, a history of goiter or thyroid nodules or a family history of thyroid cancer are also associated with an increased risk.

During 2000 through 2007, 5-year survival rates for thyroid cancer were 99.8% for localized tumors, 97.0% for regional staged tumors, and 57.3% for distant staged tumors (Table 3). The increasing incidence of thyroid cancer and high rates of survival will result in an increasingly large population of survivors and associated health care demands. Thyroid cancer incidence rates (per 100,000 population) for all races combined were 3-fold higher among women (21.0) versus men (7.0) during 2004 through 2008; this higher rate among women is believed to reflect an interaction between sex hormones and thyroid-stimulating hormone, although the precise mechanism is unknown. Thyroid cancer is also associated with benign diseases of the thyroid, which are also more common in women, and with obesity.

**Kidney and Renal Pelvis**

During 1999 through 2008, kidney and renal pelvis (referred to as kidney) cancer incidence rates significantly increased for men and women of every race/ethnicity (except American Indian or Alaska Native men) (Table 2). Kidney cancer incidence rates increased for every age group (Fig. 1). Rates increased most dramatically for localized stage tumors (from 7.6 per 100,000 population in 1999 to 12.2 per 100,000 population in 2008) (Fig. 2). Previous studies that stopped follow-up in 1995 or 1998 found increases in local and regional staged kidney cancer. However, in the current analysis from 1999 through 2008, only the incidence of localized disease increased, suggesting that these trends may be due to a greater uptake of abdominal imaging procedures (ultrasound, computed tomography, and magnetic resonance imaging), which may detect asymptomatic early stage renal cancers as incidental findings. Most of the kidney cancer cases assessed in this analysis were renal cell adenocarcinomas (accounting for 94% and 93% of all kidney cancers among men and women, respectively, during 1999-2008). In a separate analysis of renal pelvis cancers (which are mostly of the transitional cell type), there were no significant increases over time (data not shown).

Five-year survival rates for kidney cancer increased slightly over time for localized disease, from 88.4% during 1992 through 1995 to 91.1% during 2000 through 2007 (Table 3). During the corresponding time intervals, survival increased from 57.0% to 62.4% for regional disease and from 7.3% to 9.5% for distant staged disease.

Kidney cancer rates (per 100,000 population) during 2004 through 2008 were 2-fold higher among men (26.2) versus women (13.6), and were highest for black and American Indian or Alaska Native
Melanoma of the Skin

Melanoma incidence rates continued to increase among white men (2.1% per year) and white women (2.4% per year) during 1999 through 2008 (Table 2). Rates increased for men aged older than 55 years and women of all ages (Fig. 1). By stage at diagnosis, only rates of localized disease increased (from 18.0 per 100,000 population during 1999 to 22.2 per 100,000 population during 2008) (Fig. 2). Overall, the continued increases in melanoma incidence rates may reflect changing sun exposure patterns and the use of indoor tanning booths by young women, as well as increased awareness and detection practices leading to the detection of lesions that may have otherwise gone undiagnosed.\textsuperscript{53,54}

Five-year relative survival rates increased somewhat over time and were promising for local staged melanomas (99.3\% during 2000-2007). During the most recent period (2004-2008), rates (per 100,000 population) were higher among men (30.3) than among women (19.5), and by race/ethnicity and sex, rates were highest for white men (33.4) and women (22.1), reflecting differences in sun exposure and susceptibility to melanoma.

Conclusions

The increasing incidence patterns for the 7 cancers presented herein vary by sex, race/ethnicity, age, and stage at diagnosis. Reasons for these increasing trends are not entirely known, although temporal changes in risk factors (in particular the recent rise in obesity in the United States) can be plausibly linked to a number of cancers with increasing incidence rates (esophageal adenocarcinoma and pancreas, liver, and kidney cancers). In addition, the overall poor survival rates for esophageal adenocarcinoma and cancers of the pancreas and liver point to the need for improved screening, early detection, and treatment options for these often-fatal cancers. Additional research is also needed to determine the underlying causes of these increasing rates and to address factors resulting in sex and racial/ethnic disparities in cancer rates and trends. In particular, the racial differences in increasing trends for HPV-related oropharyngeal cancer and esophageal adenocarcinoma highlight the importance of examining trends in rates for etiologically distinct cancer subtypes.

As incidence and mortality rates decline for the most common cancers, the 7 cancers highlighted in this analysis will likely rise in prominence, underscoring the need for additional research and resources across the spectrum of cancer prevention, early detection, treatment, and palliation. We further note that the total number of cancer patients in the United States is expected to double to 2.6 million people by 2050 simply due to population growth and aging.\textsuperscript{55} Some of the cancers highlighted herein have promising survival rates (in particular, thyroid cancer and melanoma of the skin), and these cancers will add to the growing number of cancer survivors with complex health care and societal needs, including reduced income and productivity due to a protracted illness, economic stress, and limited or diminishing social support.\textsuperscript{56} Furthermore, as cancer survivors age, some will be at increased risk for second cancers, requiring medical surveillance. Finally, as the population of people living with cancer grows, the need for access to comprehensive cancer centers and trained medical professionals (eg, oncologists and specialized nursing staff) will also increase.\textsuperscript{57}

Strengths of this study include the use of high-quality, population-based cancer surveillance data covering over 85\% of the United States during the study period. However, a limitation is our inability to account for changes in cancer staging practices over time. In particular, trends in incidence rates by stage at diagnosis should be interpreted with caution because of the introduction of Collaborative Staging criteria in 2004, which may have affected the stage distribution for some cancers.\textsuperscript{58}

In summary, cancers with increasing incidence rates in the United States represent an area of focus for cancer prevention and control programs, researchers, and the public at large. A number of the cancers highlighted are, in part, preventable through smoking cessation and maintaining a healthy body weight. Continued monitoring of incidence rates and trends is warranted, as is additional research to determine the role of etiologic factors in the development of these cancers in order to develop appropriate screening, early detection, and treatment programs.\textsuperscript{59}
References

1. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: NAACCR Incidence-CIN Analytic File, 1973-2008, based on Expanded Races, Custom File With County, ACS Facts & Figures Projection Project, North American Association of Central Cancer Registries. Bethesda MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program, Cancer Statistics Branch. 2011. Referred April 11 based on the November 2010 submission.

2. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: Incidence-SEER 17 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2010 Sub (1973-2008 varying). Bethesda, MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program, Cancer Statistics Branch. 2011.

3. North American Association of Central Cancer Registries. NAACCR Guideline for Enhancing Hispanic-Latino Identification: Revised NAACCR Hispanic/Latino Identification Algorithm (NIHA v2.2). Available at URL: http://www.naaccr.org/LinkClick.aspx?fileticket=6dMN9F8Sc1eU%3D&tabid=92. Accessed November 1, 2011.

4. National Cancer Institute. SEER Summary Staging Manual-2000: Codes and Coding Instructions, Bethesda, MD: National Cancer Institute; 2010.

5. Howlader N, Noone AM, Krapcho M, et al, eds. SEER Cancer Statistics Review, 1975-2008. Bethesda, MD: National Cancer Institute; 2011. Available at http://seer.cancer.gov/csr/1975_2008/, based on November 2010 SEER data submission, posted to the SEER web site, 2011. Accessed November 1, 2011.

6. World Health Organization. International Classification of Diseases for Oncology, 3rd edition. Geneva: World Health Organization; 2000.

7. Chaturvedi AK, Engels EA, Anderson WF, Gillison ML. Incidence trends for human papillomavirus-related and unrelated oral squamous cell carcinomas in the United States. J Clin Oncol. 2008;26:612-619.

8. Parkin DM, Bray F, Piana S. Chapter 2: The burden of HPV-related cancers. Vaccine. 2006;24(suppl 3):S3/11-S3.25.

9. D’Souza G, Kreimer AR, Viscidi R, et al. Case-control study of human papillomavirus and oropharyngeal cancer. N Engl J Med. 2007;356:1944-1956.

10. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for jointpoint regression with applications to cancer rates. Stat Med. 2000;19:335-351.

11. Ederer F, Heise H. Instructions to IBM 650 Printing Punching-Pressing Survival Computations. Methodological Note No. 10. Bethesda, MD: National Cancer Institute; 1959.

12. Sturgis EM, Cinciripini PM. Trends in head and neck cancer incidence in relation to smoking prevalence: an emerging epidemiologic human papillomavirus-associated cancers. Cancer. 2007;110:1429-1435.

13. Gillison ML, Koch WM, Capone RB, et al. Evidence for a familial association between human papillomavirus and a subset of head and neck cancers. J Natl Cancer Inst. 2000;92:709-720.

14. Brown LM, Check DP, Devesa SS. Oropharyngeal cancer incidence trends: diminishing racial disparities. Cancer Causes Control. 2011;22:753-763.

15. Chaturvedi AK, Engels EA, Pfeiffer RM, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States [published online ahead of print October 3, 2011]. J Clin Oncol.

16. Settle K, Posner MR, Schumaker LM, et al. Racial survival disparities in head and neck cancer reveal low prevalence of human papillomavirus infection in black oropharyngeal cancer patients. Cancer Prev Res (Phila). 2009;2:776-781.

17. Brawley OW. Oropharyngeal cancer, race, and the human papillomavirus. Cancer Prev Res (Phila). 2009;2:769-772.

18. Heck JE, Berthiller J, Vaccarella S, et al. Sexual behaviours and the risk of head and neck cancers: a pooled analysis in the International Head and Neck Cancer Epidemiology (INHANCE) consortium. Int J Epidemiol. 2010;39:166-181.

19. Schiffman M, Hildesheim A. Cervical cancer. In: Schottenfeld D, Fraumeni J, eds. Cancer Epidemiology and Prevention. New York: Oxford; 2006:1044-1067.

20. FUTURE II Study Group. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. N Engl J Med. 2007;356:1915-1927.

21. Paavonen J, Naud P, Salmeron J, et al. Efficacy of human papillomavirus (HPV) 16/18 AS04-adjuvanted vaccine against cervical infection and precursor caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. Lancet. 2009;374:301-314.

22. Giuliano AR, Palefsky JM, Goldstone S, et al. Efficacy of quadrivalent HPV vaccine against HPV infection and disease in males. N Engl J Med. 2011;364:401-411.

23. Blot W, McLaughlin J, Fraumeni J, Esophageal cancer. In: Schottenfeld D, Fraumeni J, eds. Cancer Epidemiology and Prevention. New York: Oxford; 2006:763-786.

24. Varela M, Sala M, Llovet JM, Bruix J. Hepatitis C virus infection in the United States, 1999 through 2002. Ann Intern Med. 2006;144:705-714.

25. Ahmed F, Perz JF, Kwong S, Jamison PM, Friedman C, Bell BP. National trends and disparities in the incidence of hepatocellular carcinoma, 1998-2003. Prev Chronic Dis. 2008;S8:A74.

26. Kim R, Weissfeld JL, Reynolds JC, Kuller LH. Etiology of Barrett's metaplasia and adenocarcinoma. Gut. 1999;45:803-809.

27. lagereg J, Bergstrom R, Nyren O. Association between body mass and adenocarcinoma of the esophagus and gastric cardia. Ann Intern Med. 1999;130:883-890.

28. lagereg J, Bergstrom R, Lindgren A, Nyren O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. N Engl J Med. 1999;340:825-831.

29. Kim R, Weissfeld JL, Reynolds JC, Kuller LH. Etiology of Barrett’s metaplasia and adenocarcinoma. Cancer Epidemiol Biomarkers Prev. 1997;6:369-377.

30. Islami F, Kamangar F. Helicobacter pylori infection: an emerging epidemiologic association with body mass and adenocarcinoma. Cancer Epidemiol Biomarkers Prev. 2008;17:235-241.

31. Wang KK, Sampliner RE; Practice Parameters Committee of the American College of Gastroenterology. Updated guidelines 2008 for the diagnosis, surveillance and therapy of Barrett’s esophagus. Am J Gastroenterol. 2009;104:788-797.

32. Anderson KE, Mack TM, Silverman DT, Cancer of the pancreas. In: Schottenfeld D, Fraumeni J, eds. Cancer Epidemiology and Prevention. New York: Oxford; 2006:721-762.

33. Berrington de Gonzalez A, Sweetland S, Spencer E. A meta-analysis of obesity and the risk of pancreatic cancer. Br J Cancer. 2003;89:519-523.

34. Silverman DT, Hoover RN, Brown LM, et al. Why do Black Americans have a higher risk of pancreatic cancer than White Americans? Epidemiology. 2003;14:45-54.

35. Goggins M, Canto M, Hruban R. Can we screen high-risk individuals to detect early pancreatic carcinoma? J Surg Oncol. 2000;74:243-248.

36. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Ruhnet WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. Ann Intern Med. 2006;144:705-714.

37. London W, McGlynn K. Liver cancer. In: Schottenfeld D, Fraumeni J, eds. Cancer Epidemiology and Prevention. New York: Oxford; 2006:763-786.

38. Varela M, Sala M, Llovet JM, Bruix J. Hepatitis B virus infection: is there an optimal strategy? Cancer Treat Rev. 2003;29:99-104.

39. Ahmed F, Perz JF, Kwong S, Jamison PM, Friedman C, Bell BP. National trends and disparities in the incidence of hepatocellular carcinoma, 1998-2003. Prev Chronic Dis. 2008;5:A74.

40. Shepard CW, Simard EP, Finelli L, Fiore AE, Bell BP. Hepatitis B virus infection: epidemiology and vaccination. Epidemiol Rev. 2006;28:112-125.

41. Mast EE, Margolis HS, Fiore AE, et al; Advisory Committee on Immunization Practices (ACIP). A comprehensive immunization strategy to eliminate transmission of hepatitis B virus in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part I: immunization of infants, children, and adolescents. MMWR Recomm Rep. 2005;54(RR-16):1-31.

42. Mast EE, Weinbaum CM, Fiore AE, et al; Advisory Committee on Immunization Practices (ACIP). Centers for Disease Control and Prevention (CDC). A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part II: immunization of adults. MMWR Recomm Rep. 2006;55(RR-16):1-33; quiz CE1-CE4.

43. Lok AS. Does antiviral therapy for hepatitis B and C prevent hepatocellular carcinoma? J Gastroenterol Hepatol. 2011;26:221-227.

44. Bruix J, Sherman M; American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma: an update. Hepatology. 2011;53:1020-1022.

45. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. JAMA. 2006;295:2164-2167.
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46. Davies L, Ouellette M, Hunter M, Welch HG. The increasing incidence of small thyroid cancers: where are the cases coming from? *Laryngoscope*. 2010;120:2446-2451.

47. Aschebrook-Kilfoy B, Ward MH, Sabra MM, Devesa SS. Thyroid cancer incidence patterns in the United States by histologic type, 1992-2006. *Thyroid*. 2011;21:125-134.

48. Chen AY, Jemal A, Ward EM. Increasing incidence of differentiated thyroid cancer in the United States, 1988-2005. *Cancer*. 2009;115:3801-3807.

49. Enewold L, Zhu K, Ron E, et al. Rising thyroid cancer incidence in the United States by demographic and tumor characteristics, 1980-2005. *Cancer Epidemiol Biomarkers Prev*. 2009;18:784-791.

50. Ron E, Schneider A. Thyroid cancer. In: Schottenfeld D, Fraumeni J, eds. Cancer Epidemiology and Prevention. New York: Oxford; 2006:975-994.

51. Chow WH, Devesa SS, Warren JL, Fraumeni JF Jr. Rising incidence of renal cell cancer in the United States. *JAMA*. 1999;281:1628-1631.

52. Hock LM, Lynch J, Balaji KC. Increasing incidence of all stages of kidney cancer in the last 2 decades in the United States: an analysis of surveillance, epidemiology and end results program data. *J Urol*. 2002;167:57-60.

53. Jemal A, Devesa SS, Hartge P, Tucker MA. Recent trends in cutaneous melanoma incidence among whites in the United States. *J Natl Cancer Inst*. 2001;93:678-683.

54. Purdue MP, Freeman LE, Anderson WF, Tucker MA. Recent trends in incidence of cutaneous melanoma among US Caucasian young adults. *J Invest Dermatol*. 2008;128:2905-2908.

55. Edwards BK, Howe HL, Ries LA, et al. Annual report to the nation on the status of cancer, 1973-1999, featuring implications of age and aging on U.S. cancer burden. *Cancer*. 2002;94:2766-2792.

56. National Cancer Institute. Voices of a Broken System: Real People, Real Problems. President’s Cancer Panel: Report of the Chairman 2000-2001. Bethesda, MD: National Institutes of Health; 2001.

57. American Society of Clinical Oncology. Forecasting the Supply of and Demand for Oncologists: A Report to the American Society of Clinical Oncology (ASCO) from the AAMC Center for Workforce Studies. Available at URL: http://www.asco.org/ASCO/Downloads/Cancer%20Research/Oncology%20Workforce%20Report%20FINAL.pdf. Accessed November 1, 2011.

58. Wu XC, Yu Q, Andrews PA, et al. Comparisons of directly coded SEER Summary Stage 2000 and Collaborative Staging Derived SEER Summary Stage 2000. *J Registry Manag*. 2010;37:137-140.