Special Section: Cancers with Increasing Incidence Trends in the US: 1999-2008

Introduction

The incidence rates of many cancers have declined in recent years due to numerous factors. Decreases in smoking have manifested as declines in lung cancer incidence rates among men, and more recently among women.[1] Colorectal and cervical cancer incidence rates have declined due in part to early detection and removal of precancerous lesions.[2] The incidence of stomach cancer has declined due to a decreasing prevalence of *Helicobacter pylori* infection associated with improved hygiene and overall improvements in diet and food storage practices.[3] More recently, declines in prostate cancer incidence may be associated with a plateau in prostate-specific antigen (PSA) screening among men. Female breast cancer incidence rates have remained stable after declining 7% from 2002 to 2003, largely due to reductions in the use of hormone replacement therapy, an important risk factor for breast cancer.[4]

Despite these improvements in incidence trends for the major cancer sites, incidence rates for several cancers are increasing, including: human papillomavirus (HPV)-related oropharyngeal cancer; esophageal adenocarcinoma; melanoma of the skin; and cancers of the pancreas, liver and intrahepatic bile duct, thyroid, and kidney and renal pelvis. The causes of these increasing incidence trends are unclear, but may reflect the combined effects of changes in cancer risk factors and detection practices. Notably, as the US population continues to shift to older age groups where cancer risk is highest, if rates of other more common cancers remain unchanged or decline, cancers with increasing trends will account for a greater proportion of all cancer cases over time.[5]

The purpose of this special section is to highlight cancers with increasing incidence rates among people 15 years of age or older and to describe trends by age, race/ethnicity, and stage at diagnosis. This information is intended to inform communities, policy makers, researchers, and private and governmental health agencies charged with cancer prevention and control. Additional information for most of these cancers, including estimated numbers of new cases and deaths, signs and symptoms, and treatment, can be found in Selected Cancers, beginning on page 9 of this report.

Data and Methods

Cancer incidence rates are based on surveillance data from the North American Association of Central Cancer Registries (NAACCR),[6] a compilation of population-based incidence data from the National Cancer Institute's Surveillance, Epidemiology and End Result program and the Centers for Disease Control and Prevention's National Program of Cancer Registries. Average incidence rates per 100,000 population are reported by gender and race/ethnicity for the most recent five-year period combined (2004-2008). Trends in rates were assessed for the most recent 10-year period (1999-2008) and expressed as the average annual percentage change (AAPC). Average five-year incidence rates during 2004-2008 are also reported by state and gender to inform local cancer control programs. Average annual incidence rates by stage at cancer diagnosis and five-year relative survival rates are also presented to assess trends over time.[7]

HPV-related Oropharynx

The oropharynx is the part of the throat just behind the mouth. It includes the back one-third of the tongue, the soft palate (back of the roof of mouth), the tonsils, and the side and back walls of the throat. Most oropharyngeal cancers are called squamous cell carcinomas because they begin in squamous cells – the cells that line the mouth and throat. Oropharyngeal cancers can be categorized as human papillomavirus (HPV) related or unrelated, based on whether the tumor tests positive for HPV. Most oropharyngeal cancers that are not caused by HPV infection are due to tobacco and alcohol use.[8]

Risk factors: Although there are many different types of HPV, most (90%) HPV-related oropharyngeal cancers are due to infection with the HPV 16 subtype.[9,10] Prior infection with HPV 16 is associated with a nine-fold increased risk of oropharyngeal cancer, specifically for squamous cell carcinomas of the base of the tongue, tonsil, and epiglottis.[11] Sexual behaviors as well as open-mouth kissing are important routes of exposure to oral HPV infection.[12] Risk of oral HPV infection is also increased among smokers. Persistent HPV infection of the oral cavity may lead to genetic damage and altered immune function, promoting progression to cancer.

Rates and trends: During 1999-2008, 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; however, there were no significant changes among men and women of other racial and ethnic groups (Table 1). Incidence rates increased among men in all age groups and among women for those 15-64 years of age (Figure 1, A). By stage, rates increased for regional-

Table 1. Rates (2004-2008) and Trends (1999-2008) for Cancers with Increasing Incidence by Race/Ethnicity and Sex, Ages 15 Years and Older, US

	Overall		White		African American		Asian or Pacific Islander		American Indian or Alaska Native		Hispanic/ Latino†	
	Rate	AAPC	Rate	AAPC	Rate	AAPC	Rate	AAPC	Rate	AAPC	Rate	AAPC
Male												
HPV-related oropharynx	7.8	3.9*	8.0	4.4*	8.0	-0.1	2.1	0.7	4.1	-0.1	4.4	0.3
Esophageal adenocarcinoma	7.2	1.7*	8.0	1.8*	1.8	0.9	1.3	4.0	3.6	-0.1	3.7	2.8*
Pancreas	17.1	0.8*	16.8	0.9*	21.3	0.5	12.3	0.3	11.8	-0.2	14.6	0.3
Liver & intrahepatic bile duct	12.3	3.9*	10.9	3.8*	17.9	5.4*	27.6	-0.2	17.4	3.4	21.5	2.4*
Thyroid	7.0	6.2*	7.4	6.3*	3.8	5.6*	6.3	5.0*	3.1	0.6	5.4	4.5*
Kidney & renal pelvis	26.2	2.4*	26.3	2.3*	28.5	3.1*	12.5	3.5*	29.4	1.9	24.5	2.0*
Melanoma of the skin	30.3	2.1*	33.4	2.1*	1.4	-0.1	2.0	0.0	4.6	0.3	5.9	-0.3
Female												
HPV-related oropharynx	1.7	1.6*	1.8	1.9*	1.7	-0.6	0.5	-2.2	0.8	NA	0.9	-0.7
Esophageal adenocarcinoma	1.0	1.9*	1.1	2.1*	0.5	1.0	0.3	6.4	0.9	3.2	0.6	-1.1
Pancreas	13.2	0.9*	12.8	1.0*	17.6	0.4	10.3	-0.4	11.5	-0.4	12.6	0.2
Liver & intrahepatic bile duct	4.1	1.9*	3.7	1.5	5.1	2.7*	10.4	0.2	8.5	4.4	8.1	1.0
Thyroid	21.0	7.3*	21.6	7.3*	12.6	6.8*	21.5	6.4*	10.0	3.1*	20.4	6.7*
Kidney & renal pelvis	13.6	2.9*	13.7	2.8*	14.6	3.8*	6.1	3.7*	17.0	3.4*	14.0	2.7*
Melanoma of the skin	19.5	2.3*	22.1	2.4*	1.3	1.0	1.6	-1.9	4.0	1.9	5.4	0.2

AAPC = average annual percent change from 1999 to 2008. HPV = human papillomavirus. NA = trend could not be calculated due to sparse data.Incidence rates are per 100,000 population and were age-adjusted to the 2000 US standard population. *AAPC is significantly different from zero (p <0.05). †Persons of Hispanic origin may be of any race.

Source: North American Association of Central Cancer Registries (NAACCR) 2011. Data are collected by cancer registries participating in NCI's SEER program and CDC's National Program of Cancer Registries.

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and distant-staged tumors, but not for localized disease (Figure 2). The increasing incidence rates for HPV-related oropharyngeal cancers are in stark contrast to steady declines in rates for HPV-unrelated oropharyngeal cancers, which are largely due to decreases in smoking prevalence.[13] Reasons for these increasing rates are unclear, but may be related to changing sexual practices among men (such as an increase in the prevalence of oral sex).[12,14] The most dramatic increase in rates was among men 55-64 years of age, consistent with changes in sexual behaviors that increase risk of HPV-exposure in this population.[10] The rapid increase in whites may reflect trends in risk factors such as oral-genital sexual behavior. However, existing data do not provide a clear explanation for the observed differences by race. Additional research is needed to clarify the routes of oral HPV transmission and to develop appropriate, targeted prevention strategies.

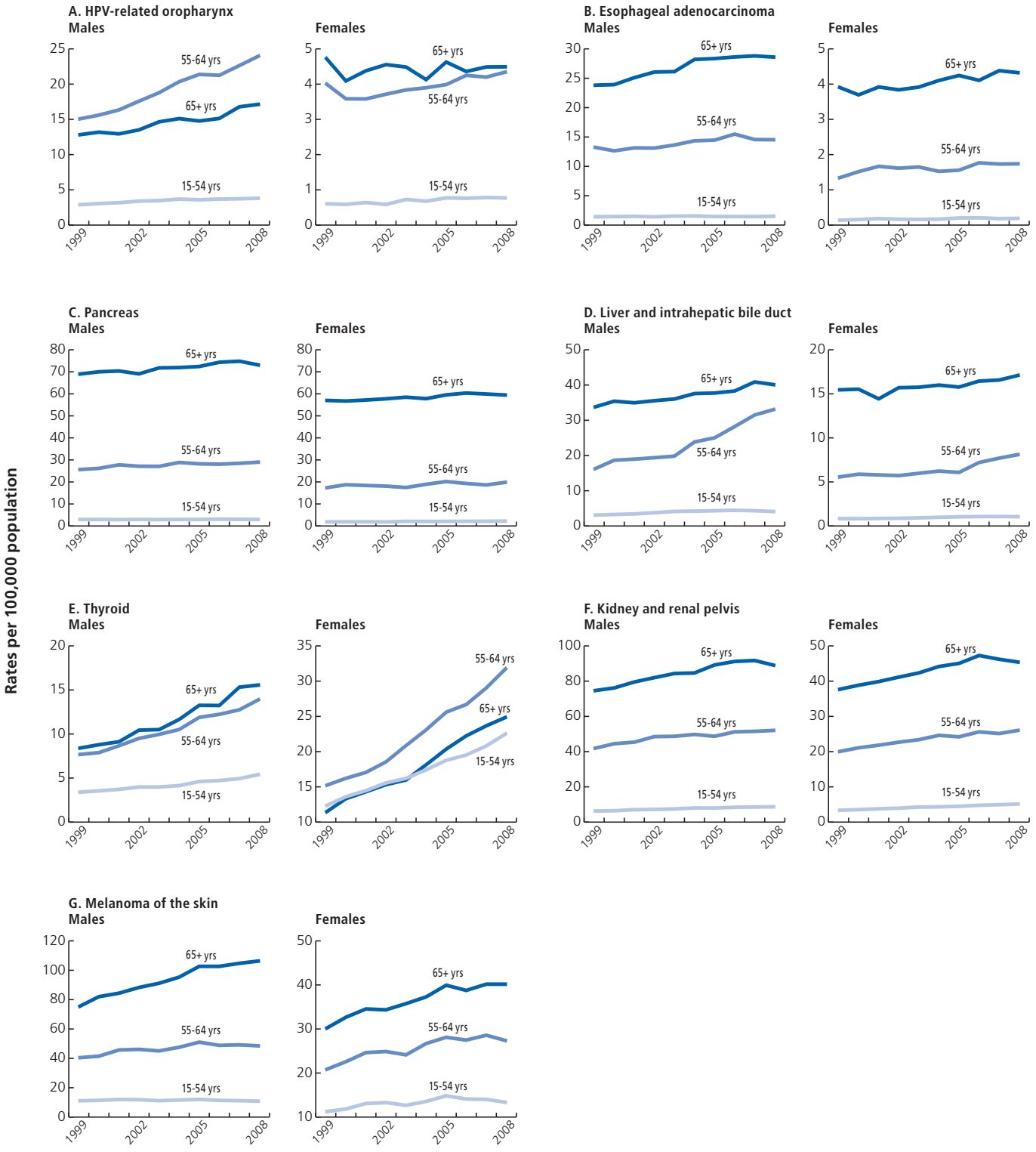
Survival: Despite the concerning trends in increasing incidence rates, survival rates for HPV-related oropharyngeal cancer are generally higher than those for HPV-unrelated oropharyngeal cancers.[10] Five-year survival rates for HPV-related oropharyngeal cancer have increased over time for each stage of diagnosis, with the largest improvement (20%) for regional disease (Table 3).

Prevention and early detection: The continued increases in incidence rates among white men and women and sustained high burden of disease among African American men suggests the need for interventions specific to these groups. Education to promote safer sexual practices (particularly oral sex), as well as continued reductions in tobacco use, may be important prevention strategies to consider. Additional research is also needed to determine if the HPV vaccine (currently recommended to prevent cervical cancer in women) might also prevent HPV-related oropharyngeal cancer among men and women.[15] The observation that incidence of regionally advanced oropharyngeal cancer was greater than less-advanced stages points to the need for improved early detection methods. Although survival was generally optimistic among those with localized tumors, poorer survival among those with advanced tumors also underscores the need for improvements in treatment.

Esophageal adenocarcinoma

Overall, esophageal cancer incidence rates have declined rapidly in African American men and women, remained unchanged in white women, and increased slightly among white men. Rates were historically higher among African Americans compared to whites, but more recently, the highest incidence is observed among non-Hispanic white men.[16,17] Although both major subtypes of

Figure 1. Incidence Rates* by Sex and Age for Cancers with Increasing Trends, 1999-2008.



HPV = human papillomavirus

*Age adjusted to the 2000 US standard population. Note the scale of the Y axis differs between cancer sites and genders.

Source: North American Association of Central Cancer Registries. Data are collected by cancer registries participating in NCI's SEER program and CDC's National Program of Cancer Registries.

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Table 2. Incidence Rates* for Cancers with Increasing Trends by State and Sex, Ages 15 Years and Older, 2004-2008

	HPV-related oropharynx		Esophageal adenocarcinoma		Pancreas		Liver & intrahepatic bile duct		Thyroid		Kidney & renal pelvis		Melanoma of the skin	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Alabama†	8.6	2.2	6.5	0.6	17.6	12.4	10.2	3.6	5.3	14.2	25.9	13.3	31.5	18.0
Alaska	7.6	1.2	7.3	1.7	17.2	14.3	14.0	6.0	7.2	22.0	26.4	15.6	14.4	12.9
Arizona	6.2	1.7	5.9	0.7	14.5	11.2	11.5	3.9	7.6	23.6	23.3	13.2	24.7	14.5
Arkansas	8.6	2.1	5.6	0.7	16.4	11.8	9.9	3.1	5.1	12.8	27.2	14.3	22.7	13.8
California	7.0	1.5	5.4	0.7	16.3	13.3	16.2	5.7	6.1	18.2	23.2	11.2	34.3	20.0
Colorado	6.5	1.3	7.4	0.9	15.0	12.8	10.5	3.8	7.4	21.4	22.5	11.5	32.3	23.5
Connecticut	7.8	1.5	7.9	1.1	20.6	14.9	13.2	3.6	9.8	29.2	26.4	13.7	37.9	25.8
Delaware	9.6	1.9	7.6	1.2	18.1	13.8	12.0	3.0	6.9	20.7	25.8	14.8	42.0	22.8
District of Columbia	8.9	3.3	4.3	0.6	19.7	12.9	17.3	4.7	7.4	15.9	21.9	10.5	15.7	7.2
Florida	9.7	2.2	6.4	0.8	16.7	12.5	12.3	3.8	6.4	18.9	24.0	12.3	30.3	17.9
Georgia	8.5	1.8	5.5	0.6	17.2	12.7	11.4	3.5	5.7	17.1	24.7	12.5	35.5	20.5
Hawaii	7.3	1.3	3.4	0.3	18.0	14.3	19.1	7.2	7.9	24.7	21.8	10.6	34.5	19.1
Idaho	7.6	1.5	8.1	1.0	16.4	13.5	8.1	2.9	7.9	28.9	22.9	12.8	38.1	23.6
Illinois	8.0	1.9	8.1	1.1	18.9	14.2	11.6	4.1	7.1	21.0	28.8	15.1	25.0	16.6
Indiana	8.1	1.8	9.3	1.1	17.0	12.7	9.5	3.4	6.0	18.1	28.3	15.9	26.6	18.1
Iowa	7.1	1.5	9.8	1.2	17.0	12.4	8.6	3.2	7.5	19.8	29.0	14.6	29.7	22.1
Kansas	6.9	1.2	7.0	0.8	15.9	12.2	8.2	2.9	8.2	24.5	25.4	13.7	31.7	22.7
Kentucky	8.8	2.1	8.4	1.0	16.6	13.1	9.8	3.7	7.1	21.4	30.6	16.3	35.2	23.8
Louisiana†	9.3	1.6	6.0	0.7	18.7	15.4	15.1	4.2	5.8	16.1	32.4	17.0	23.4	12.8
Maine	8.7	2.2	12.0	1.2	17.7	14.4	9.2	3.4	6.3	21.4	25.8	15.3	32.6	24.6
Maryland‡	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Massachusetts	8.0	1.8	10.7	1.5	17.8	14.0	14.2	3.8	10.6	31.1	28.4	13.7	35.5	23.9
Michigan	7.5	1.8	8.1	1.3	18.5	14.0	10.8	4.1	6.5	18.5	25.8	14.1	27.8	20.0
Minnesota	6.9	1.7	8.5	1.1	14.9	11.3	8.1	2.9	7.0	19.2	26.4	13.6	32.5	24.5
Mississippi†	8.9	2.0	5.3	0.6	17.8	12.6	11.6	3.8	5.6	14.6	30.1	15.5	25.4	15.2
Missouri	8.8	1.8	7.8	1.0	17.3	13.2	11.5	3.6	6.8	19.7	29.5	15.0	28.4	17.3
Montana	6.8	1.5	8.4	1.1	16.2	12.2	6.7	3.3	6.5	22.9	21.2	11.0	26.0	21.0
Nebraska	6.4	1.2	8.4	1.0	17.7	12.3	8.5	2.9	6.9	22.9	25.9	15.0	27.6	19.2
Nevada	6.3	2.1	6.9	0.8	16.3	13.5	11.3	4.8	7.7	23.0	22.6	11.5	26.5	14.4
New Hampshire	7.7	2.2	12.3	1.8	16.9	14.7	8.3	2.4	8.0	24.7	24.4	12.3	43.2	30.3
New Jersey	6.9	1.6	7.0	1.1	18.8	14.3	12.7	4.2	9.1	27.2	27.4	13.4	34.5	22.6
New Mexico	5.1	1.2	5.8	0.6	15.0	12.0	15.3	5.5	7.3	23.9	21.1	11.7	28.9	17.8
New York	6.9	1.5	6.7	1.2	18.7	14.7	15.5	4.7	8.7	25.1	27.4	13.0	25.9	16.2
North Carolina	9.3	2.0	6.7	0.9	16.5	13.4	10.8	3.4	6.7	19.4	29.8	13.6	32.6	20.5
North Dakota	5.8	1.1	7.3	1.5	18.0	11.9	6.3	2.9	7.0	22.9	25.6	13.4	22.4	21.6
Ohio	7.7	1.9	9.1	1.3	17.2	12.9	9.3	3.1	6.1	18.8	25.8	14.8	28.7	21.5
Oklahoma	8.0	1.9	7.4	0.8	16.1	12.0	11.3	4.5	5.0	15.6	27.2	15.1	30.5	19.2
Oregon	8.6	1.7	9.1	1.1	15.7	13.4	11.0	3.9	6.5	19.0	24.4	12.7	38.2	30.3
Pennsylvania	7.5	1.7	9.0	1.3	18.4	14.1	12.5	3.6	9.3	30.2	28.4	14.7	27.5	19.3
Rhode Island	8.0	2.2	10.3	1.5	16.4	12.1	14.3	4.4	10.0	28.7	29.5	15.3	33.8	23.8
South Carolina	9.0	2.1	5.6	0.7	16.9	13.1	10.0	2.8	4.9	15.4	24.4	13.5	34.7	22.2
South Dakota	4.5	1.1	8.5	1.1	14.2	11.2	5.8	2.2	5.4	18.5	23.3	13.9	20.9	16.2
Tennessee	8.2	2.0	6.2	0.9	16.0	12.0	10.0	3.2	6.9	19.4	26.6	14.0	32.0	19.9
Texas†	7.6	1.6	6.1	0.7	16.4	12.5	16.7	5.6	6.7	19.0	28.3	15.6	23.2	12.9
Utah	5.0	0.6	6.3	0.5	13.6	10.9	6.6	2.4	8.4	26.8	17.2	10.5	46.5	26.7
Vermont	9.6	1.7	8.7	1.5	17.2	14.7	9.3	2.8	7.1	24.6	24.8	13.5	41.9	34.2
Virginia	8.0	1.6	6.5	0.8	16.9	13.2	11.1	3.6	6.2	17.3	24.9	12.4	33.8	20.3
Washington	7.9	1.5	7.9	1.3	16.8	13.8	12.3	4.7	7.2	20.6	25.4	13.4	37.1	28.2
West Virginia	8.6	2.4	8.8	1.2	16.0	11.3	8.6	3.6	7.1	20.1	27.5	15.5	29.1	20.0
Wisconsin	7.1	1.9	8.7	1.4	17.7	13.1	10.3	4.0	6.1	18.2	26.5	14.0	26.7	18.9
Wyoming	6.7	1.7	9.2	1.2	14.3	11.4	7.5	3.3	7.4	27.1	24.2	11.6	29.6	23.8

HPV = human papillomavirus. *Per 100,000, age adjusted to the 2000 US standard population. †Data for 2005 are limited to cases diagnosed from January-June due to the effect of large migrations of populations on this state as a result of Hurricane Katrina in September 2005. ‡Data from this state are not available.

Source: North American Association of Central Cancer Registries. Data are collected by cancer registries participating in NCI's SEER program and CDC's National Program of Cancer Registries.

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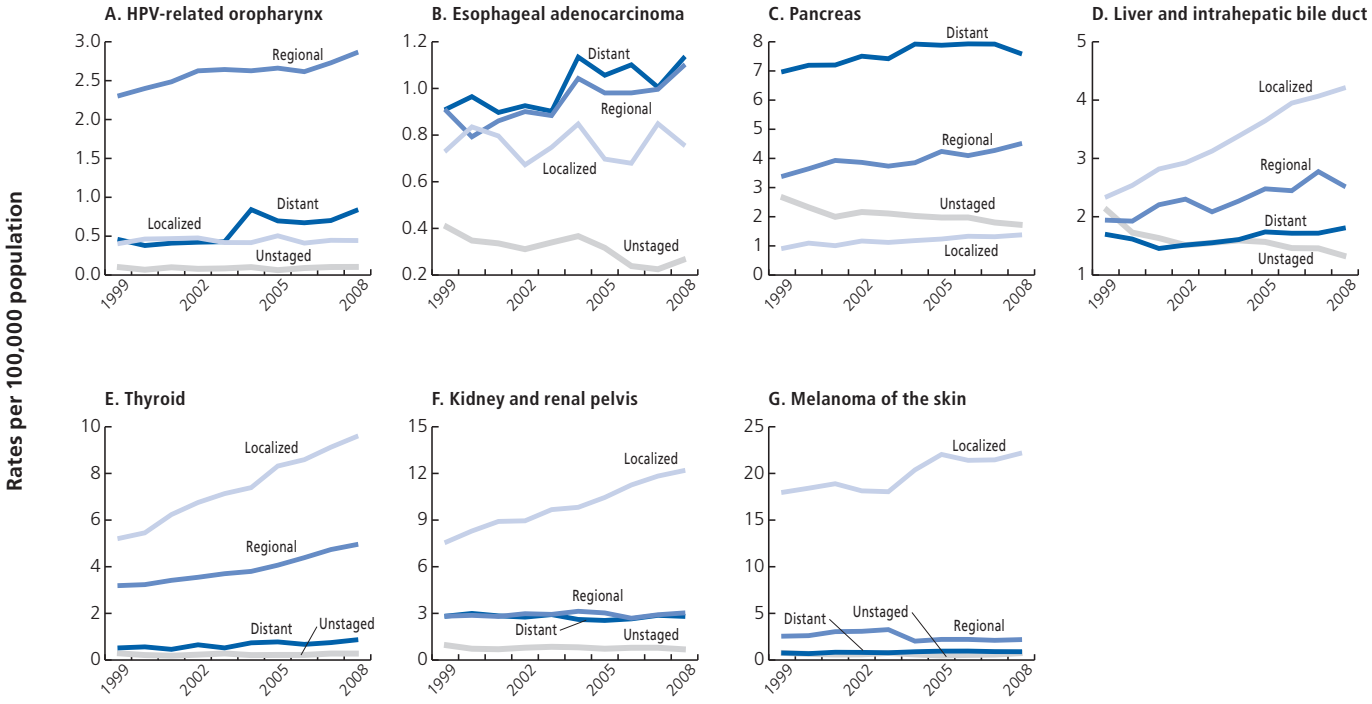
Figure 2. Incidence Rates* by Stage at Diagnosis for Cancers with Increasing Trends, Ages 15 years and older, 1999-2008.



HPV = human papillomavirus

*Age adjusted to the 2000 US standard population. Note the scale of the Y axis differs between cancer sites and genders. 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 impacted the stage distribution for some cancers.

Source: Surveillance, Epidemiology, and End Results (SEER) Program, SEER 13 database 1992-2008. National Cancer Institute.

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esophageal cancer (squamous cell carcinoma and adenocarcinoma) are related to smoking, decreases in smoking prevalence have only manifested declines in squamous cell carcinoma of the esophagus.

Risk factors: Obesity is associated with a 16-fold increased risk of esophageal adenocarcinoma.[18] Gastroesophageal reflux also increases risk through the establishment of Barrett's esophagus, a premalignant condition that can progress to esophageal adenocarcinoma.[19,20] Abdominal obesity is associated with both gastroesophageal reflux and Barrett's esophagus, possibly by increasing intra-abdominal pressure promoting acid reflux, which can initiate the malignant transformation of esophageal cells.[21] Current and former smoking is also associated with a two-fold increased risk of esophageal adenocarcinoma.[21]

Rates and trends: Incidence rates for esophageal adenocarcinoma increased significantly among white men (1.8% per year), white women (2.1% per year), and Hispanic men (2.8% per year) during 1999-2008, while there were no significant changes for men or women of other racial/ethnic groups (Table 1). Overall rates increased in men and women 55 years of age or older (Figure 1, B) and for distant- and regional-staged disease (Figure 2, B). These increasing trends coincide with rises in obesity and gastroesophageal reflux disease.[22] However, the extent to which increasing obesity rates contribute to the increasing trends and higher burden in whites is unclear because obesity prevalence has increased in men and women of all racial/ethnic groups and because obesity prevalence is highest among African Americans.[23] Rather, these patterns may reflect the higher prevalence of abdominal obesity among whites.[24]

Survival: Five-year survival rates for esophageal adenocarcinoma increased from 33.5% in 1992-1995 to 49.3% in 2001-2007 for local-staged tumors, and from 9.4% to 20.6% for regional-staged tumors. Survival was poor for distant-staged tumors, with a five-year relative survival rate of 2.8% during 2001-2007 (Table 3).

Prevention and early detection: Maintaining a healthy body weight may reduce the risk for esophageal adenocarcinoma. Treatment of gastroesophageal reflux disease with proton-pump inhibitors, which reduces gastric acid, thereby slowing or preventing the development of Barrett's esophagus, may also lower risk, although the most effective regimen to reduce cancer

Table 3. Trends in Five-year Relative Survival Rates (%) for Cancers with Increasing Incidence by Stage at Diagnosis, Ages 15 Years and Older, 1992-2007

	Localized		Regional		Distant	
	1992-1995	2001-2007	1992-1995	2001-2007	1992-1995	2001-2007
HPV-related oropharynx	63.3	78.3	47.3	66.7	21.7	37.2
Esophageal adenocarcinoma	33.5	49.3	9.4	20.6	1.9	2.8
Pancreas	15.4	21.9	6.3	9.1	1.6	1.8
Liver & intrahepatic bile duct	12.5	27.4	5.8	8.8	1.6	2.5
Thyroid	99.4	99.7	94.5	97.0	60.5	57.3
Kidney & renal pelvis	88.4	91.1	60.0	62.7	7.3	10.1
Melanoma of the skin	96.1	99.5	58.9	66.1	11.9	14.8

HPV = human papillomavirus.

Source: Surveillance, Epidemiology, and End Results (SEER) Program, SEER 13 database 1992-2008. National Cancer Institute.

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risk in these patients is not known.[21] In addition, medical surveillance for people diagnosed with Barrett's esophagus to monitor for the development of esophageal adenocarcinoma may also be beneficial; however, the timing and frequency of such screening is unclear.[25]

Pancreas

Pancreatic cancer is one of the most deadly forms of cancer and the fourth leading cause of cancer death among men and women.

Risk factors: Cigarette smoking accounts for 25%-30% of pancreatic cancer cases and confers about a two-fold increased pancreatic cancer risk relative to nonsmokers.[26] Cigar and pipe smoking, as well as use of smokeless tobacco, are also associated with elevated risks. Obesity is another important modifiable risk factor for pancreatic cancer, and obese individuals have a 20% increased risk relative to normal-weight individuals.[27] Additional risk factors include inherited genetic disorders, preexisting diabetes, and a history of pancreatitis.

Rates and trends: Increases in pancreatic cancer incidence rates were limited to white men (0.9% per year) and white women (1.0% per year) during 1999-2008 (Table 1). Incidence rates increased for men 55 years of age or older and for women of all ages, as well as for local-, regional-, and distant-staged tumors, though these increase were likely limited to whites (Figures 1, C and 2, C). Increases in obesity prevalence are thought to contribute to the rising incidence rates.[26,27] However, the prevalence of obesity has increased among all racial/ethnic groups, suggesting the presence of other factors resulting in increasing pancreatic cancer rates among white men and women only.[23]

During 2004-2008, pancreatic cancer incidence rates (per 100,000) were highest among African American men (21.3) and women (17.6), and second highest among white men (16.8) and women (12.8) (Table 1). The racial disparity in the burden of pancreatic cancer has been explained in part by higher rates of cigarette smoking and diabetes mellitus among African American men versus white men and elevated body mass index among African American women versus white women.[28]

Survival: Five-year survival for pancreatic cancer was poor regardless of stage and improved little over time. During the most recent time period (2001-2007), the five-year survival rate was 21.9% for local-staged cancer, 9.1% for regional-staged cancer, and 1.8% for distant-staged cancer. The overall poor survival for pancreatic cancer underscores the lack of effective treatments for this malignancy (Table 3).

Prevention and early detection: Avoiding tobacco use is important in the prevention of pancreatic cancer.[26] Risk can also be reduced by maintaining a healthy weight throughout life.[26] There is no recommended screening procedure for pancreatic cancer, and symptoms do not usually appear until the disease has spread to distant organs, creating a challenge for early detection.

Liver and intrahepatic bile duct

Surveillance reporting for liver cancer includes hepatocellular carcinoma (HCC), the major subtype of liver cancer accounting for approximately 80% of all cases, and tumors of the intrahepatic bile duct (cholangiocarcinomas).[29]

Risk factors: Chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) can lead to fibrosis and cirrhosis (scarring) of the liver, which dramatically increases risk of HCC. Among people with chronic HBV infection, the lifetime risk of liver cancer is 10%-25%, and these cases account for approximately 16% of all liver cancers in the US. [29,30] Among people with chronic HCV infection, there is an estimated 17-fold increased risk of HCC, and these cases account for approximately 48% of liver cancers occurring in the US.[30,31] In other parts of the world where these infections are more common, they account for a greater proportion of liver cancers. Other important risk factors for liver cancer include alcohol-induced liver disease, smoking, obesity, and diabetes.[29,32,33] A recent study found an increased

risk associated with metabolic syndrome, which reflects the interaction between obesity, diabetes, and hypertension and underscores the complex nature of multiple shared risk factors for these cancers.[34] The following sections refer to the combined group of liver and intrahepatic bile duct malignancies as "liver cancer."

Rates and trends: Significant increases in liver cancer incidence rates were observed among white (3.8% per year), African American (5.4% per year), and Hispanic men (2.4% per year) and among African American women (2.7% per year) during 1999-2008 (Table 1). Incidence rates increased for all age groups, most notably for men 55-64 years of age (Figure 1, D). Liver cancer incidence rates increased for all stages at diagnosis, although most notably for localized disease, from 2.3 (per 100,000) in 1999 to 4.2 in 2008 (Figure 2). The increasing burden of liver cancer among African American men and women, and white men, is consistent with an aging cohort of people infected with HCV through injection drug use in the past who are now reaching ages at which liver cancer risk is highest.[35]

Incidence rates continue to be highest among Asian or Pacific Islander men (27.6 per 100,000 population) and women (10.4 per 100,000 population), consistent with the substantial burden of endemic HBV infection among Asian and Pacific Islanders born elsewhere who emigrated to the US (Table 1).[36,37] The increasing incidence trends and high burden of disease in some population subgroups warrant continued monitoring as rates may continue to rise.

Survival: Five-year survival for localized liver cancer increased from 12.5% during 1992-1995 to 27.4% during 2001-2007 (Table 3). There was little improvement in five-year survival for regional- (5.8% during 1992-1995 to 8.8% during 2001-2007) or distant- (1.6% during 1992-1995 to 2.5% during 2001-2007) staged liver cancers.

Prevention and early detection: Hepatitis B vaccination, which prevents chronic HBV infection and thus HBV-related liver cancer, is recommended for all newborn children, with catch-up vaccination recommended for adolescents.[38] Hepatitis B vaccination is also recommended for high-risk adults (such as health care workers and people who inject drugs).[39] Both HBV and HCV are transmitted through injection drug use, so safe injection practices (using a sterile needle, not sharing injection drug equipment) may reduce transmission. Risk of sexual transmission of HBV and HCV may also be reduced by proper and consistent condom use. Antiviral treatment for those with chronic HBV or HCV infections also reduces liver cancer risk.[40] Risk can also be decreased by limiting alcohol intake and not smoking. Finally, maintaining a healthy body weight also decreases risk of liver cancer. Persons at high risk for liver cancer (for example, those with HBV- or HCV-related cirrhosis) may be screened every six months via ultrasound, although the effectiveness of such screening is unclear.[41]

Thyroid

Risk factors: Childhood exposure to ionizing radiation is a strong risk factor for thyroid cancer, with risk increasing with greater levels of exposure.[42] Goiter and benign thyroid nodules, as well as certain genetic characteristics, are also risk factors.[43] Thyroid cancer is more common among women than men, and various female hormonal and reproductive factors have been investigated, including miscarriage as a first pregnancy and later age at first birth.[44] These risk factors are weakly associated with thyroid cancer risk, with the associations stronger for younger versus older women, suggesting an additional role of age-specific sex hormone changes. Certain genetic factors also increase the risk of thyroid cancer.

Rates and trends: Thyroid cancer incidence rates significantly increased among men and women of every racial/ethnic background except American Indian or Alaska Native men during 1999-2008 (Table 1). Rates increased for men and women of all ages, most notably for women 55-64 years of age (Figure 1). Incidence rates (per 100,000 population) increased for tumors of all stages, although the greatest increase was for localized disease (from 5.2 in 1999 to 9.6 in 2008) (Figure 2). Reasons for these increases are not known. Some studies suggested the increasing rates are due to detection of small tumors (through ultrasound and confirmation via fine needle aspiration),[45,46] while other, more recent studies argue that the increase is in part real, and involves both small and large tumors.[47-49]

Survival: During 2001-2007, five-year survival rates were 99.7% for localized tumors, 97.0% for regional-staged tumors, and 57.3% for distant-staged tumors (Table 3).

Prevention and early detection: People with genetic risk factors for thyroid cancer may have their thyroid removed to prevent cancer.[42] There are no clear recommendations to prevent thyroid cancer or established early detection methods.

Kidney and renal pelvis

Risk factors for kidney and renal pelvis cancers are somewhat different, although the two cancers are typically combined for surveillance purposes, as they are for the incidence and survival statistics presented herein.

Risk factors: Cigarette smoking is a risk factor for kidney and renal pelvis cancers, though smoking is most strongly associated with renal pelvis cancer. Risk increases with both quantity and duration of smoking. For kidney cancer, smoking accounts for approximately 20%-30% of cases among men (conferring a 54% increased risk) and approximately 10%-20% of cases among women (conferring a 22% increased risk).[50] For cancer of the renal pelvis, smoking accounts for approximately 70%-82% of cases among men and approximately 37%-61% of cases among women.[51] Obesity also increases risk of kidney cancer, and accounts for 30%-40% of cases.[50,51] Hypertension (high blood pressure) also

increases risk of kidney cancer. There are also inherited forms of kidney cancer, which account for a small fraction of cases.

Rates and trends: During 1999-2008, kidney cancer incidence rates significantly increased for men and women of every race/ethnicity except American Indian or Alaska native men, for every age group, and most dramatically for localized tumors from 7.6 (per 100,000) in 1999 to 12.2 in 2008 (Table 1, Figures 1, F and 2, F). Previous studies analyzing data through 1995 or 1998 found increases in local- and regional-staged kidney cancer.[52, 53] However, in the current analysis from 1999 through 2008, only incidence of localized disease increased, suggesting that these trends may be due to greater uptake of imaging procedures (ultrasound, computed tomography, and magnetic resonance imaging), which detect asymptomatic early stage cancers that may have otherwise gone undiagnosed.

Rates (per 100,000) during 2004-2008 rates were two-fold higher among men (26.2) than among women (13.6), and highest for African American and American Indian or Alaska Native men (28.5 and 29.4, respectively), perhaps reflecting the higher prevalence of obesity in these populations (Table 1).

Survival: The five-year survival rate for kidney cancer increased slightly over time for localized disease, from 88.4% during 1992-1995 to 91.1% during 2001-2007 (Table 3). Survival for regional-staged kidney cancer also increased slightly from 60.0% (1992-1995) to 62.7% (2001-2007) and for distant-staged disease from 7.3% (1992-1995) to 10.1% (2001-2007).

Prevention and early detection: Avoiding smoking and maintaining a healthy weight throughout life are likely important preventive steps for kidney cancer. In addition, avoiding hypertension (through diet and exercise) and treatment of existing hypertension are also likely preventive measures.

Melanoma of the skin

Melanoma is the deadliest form of skin cancer, and is more common among whites of European descent than other racial and ethnic groups.

Risk factors: The major risk factor for melanoma of the skin is exposure to ultraviolet light. Immunosuppression, which is common among organ transplant recipients and those with HIV infection and autoimmune diseases, is also a risk factor. Exposure to ionizing radiation and some chemicals may also increase risk. People with fair skin, freckles, and/or moles and those with a family history of skin cancer and certain genetic markers may also be at increased risk for melanoma.[54] In the following section melanoma of the skin is referred to as "melanoma."

Rates and trends: Melanoma incidence rates continued to increase among white men (2.1% per year) and white women (2.4% per year) during 1999-2008 (Table 1). Rates increased for men over 55 years of age and for women of all ages (Figure 1). By stage at diagnosis, only rates of localized disease increased (from 18.0 per 100,000 in 1999 to 22.2 per 100,000 in 2008) (Figure 2). Other studies have shown that rates have increased for both thin and thick lesions.[55] 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.[55,56]

Melanoma incidence rates in whites are 5 times higher than in Hispanics and 20 times higher than in African Americans. During the most recent period (2004-2008), rates (per 100,000) were higher among men (30.3) than among women (19.5) (Table 1), reflecting differences in sun exposure.

Survival: Five-year survival rates for melanoma increased slightly for localized disease from 96.1% (1992-1995) to 99.5% (2001-2007), for regional-staged disease from 58.9% (1992-1995) to 66.1% (2001-2007), and for distant-staged disease from 11.9% (1992-1995) to 14.8% (2001-2007) (Table 3).

Prevention and early detection: Strategies to reduce risk of certain types of melanoma include proper and consistent use of sunscreen, wearing sun-protective clothing, seeking shade, and avoiding tanning beds.[54] In addition to individual-level policies, community-level policies that restrict access to tanning beds for minors and facilitate sun-safe behaviors among children are also likely to be important. Finally, increased melanoma awareness among both individuals and health care providers may also increase early detection of cancerous lesions, leading to successful treatment.

Future challenges

In 2012, cancers with increasing incidence rates are expected to account for approximately 135,000 new cancer cases among men and 110,000 cases among women. Increasing incidence of esophageal adenocarcinoma and cancers of the pancreas and liver is particularly concerning because of their poor survival, highlighting the need for early detection and treatment options for these highly fatal cancers. Additional studies are needed to determine the underlying causes of the observed increases in incidence rates for the seven cancers discussed and to address the determinants of gender and racial/ethnic differences in incidence rates and trends. While temporal trends in risk factors (in particular, the recent rise in obesity in the US) can be plausibly linked to a number of these cancers, other factors, such as increased diagnostic imaging may also be important, although the precise nature and relative contribution of these and other factors remains unclear.

Research into cancer biology utilizing genome-wide association studies may yield important etiologic findings for some cancers with strong genetic risks.[57] In addition, identification of bio-

markers of tumor aggressiveness may enable more individualized treatment options. The extensive efforts to develop personalized and/or targeted therapies hold some promise as they take into account the complex molecular composition and gene expression profiles of individual tumors.[58-60] Additionally, the development of improved early detection techniques and screening guidelines for specific high-risk populations are also important future considerations. However, the most prudent cancer prevention activities include avoiding tobacco use and obesity and increasing physical activity.

Due to population growth and aging, the number of new cancer patients is expected to double to 2.6 million people by 2050.[5] This number could further increase if the trends for cancers that are increasing are not reversed. Further, as survival from some of the cancers highlighted in this special section was generally good (in particular, thyroid cancer and melanoma of the skin), this will add to the growing population of cancer survivors with complex health care and societal needs, including reduced income and productivity due to a prolonged illness, economic stress, and limited or diminishing social support.[61] In addition, as cancer survivors age, some will be at increased risk for second cancers, requiring additional medical surveillance. The need will also grow for access to comprehensive cancer centers, for trained medical professionals (oncologists, specialized nursing staff, and others), and for health officials to develop appropriate plans to meet these needs.[62]

In summary, cancers with increasing incidence rates in the US represent an area of focus for cancer prevention and control programs and the public at-large. A number of these cancers are preventable through smoking cessation and avoidance of obesity. However, additional research is needed to determine the role of other factors and to develop appropriate screening, early detection, and treatment programs to reduce pain and suffering from these cancers.

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