

Annual Report to the Nation on the Status of Cancer, 1975-2012, Featuring the Increasing Incidence of Liver Cancer

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BACKGROUND: Annual updates on cancer occurrence and trends in the United States are provided through an ongoing collaboration among the American Cancer Society (ACS), the Centers for Disease Control and Prevention (CDC), the National Cancer Institute (NCI), and the North American Association of Central Cancer Registries (NAACCR). This annual report highlights the increasing burden of liver and intrahepatic bile duct (liver) cancers. **METHODS:** Cancer incidence data were obtained from the CDC, NCI, and NAACCR; data about cancer deaths were obtained from the CDC's National Center for Health Statistics (NCHS). Annual percent changes in incidence and death rates (age-adjusted to the 2000 US Standard Population) for all cancers combined and for the leading cancers among men and women were estimated by jointpoint analysis of long-term trends (incidence for 1992-2012 and mortality for 1975-2012) and short-term trends (2008-2012). In-depth analysis of liver cancer incidence included an age-period-cohort analysis and an incidence-based estimation of person-years of life lost because of the disease. By using NCHS multiple causes of death data, hepatitis C virus (HCV) and liver cancer-associated death rates were examined from 1999 through 2013. **RESULTS:** Among men and women of all major racial and ethnic groups, death rates continued to decline for all cancers combined and for most cancer sites; the overall cancer death rate (for both sexes combined) decreased by 1.5% per year from 2003 to 2012. Overall, incidence rates decreased among men and remained stable among women from 2003 to 2012. Among both men and women, deaths from liver cancer increased at the highest rate of all cancer sites, and liver cancer incidence rates increased sharply, second only to thyroid cancer. Men had more than twice the incidence rate of liver cancer than women, and rates increased with age for both sexes. Among non-Hispanic (NH) white, NH black, and Hispanic men and women, liver cancer incidence rates were higher for persons born after the 1938 to 1947 birth cohort. In contrast, there was a minimal birth cohort effect for NH Asian and Pacific Islanders (APIs). NH black men and Hispanic men had the lowest median age at death (60 and 62 years, respectively) and the highest average person-years of life lost per death (21 and 20 years, respectively) from liver cancer. HCV and liver cancer-associated death rates were highest among decedents who were born during 1945 through 1965. **CONCLUSIONS:** Overall, cancer incidence and mortality declined among men; and, although cancer incidence was stable among women, mortality declined. The burden of liver cancer is growing and is not equally distributed throughout the population. Efforts to vaccinate populations that are vulnerable to hepatitis B virus (HBV) infection and to identify and treat those living with HCV or HBV infection, metabolic conditions, alcoholic liver disease, or other causes of cirrhosis can be effective in reducing the incidence and mortality of liver cancer. *Cancer* 2016;122:1312-37. © 2016 American Cancer Society.

KEYWORDS: cancer, incidence, liver cancer, mortality, National Program of Cancer Registries (NPCR), North American Association of Central Cancer Registries (NAACCR), Surveillance, Epidemiology, and End Results (SEER), survival, trends, viral hepatitis.

INTRODUCTION

This marks the 18th year that the American Cancer Society (ACS), the Centers for Disease Control and Prevention (CDC), the National Cancer Institute (NCI), and the North American Association of Central Cancer Registries

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See Editorial on pages 1343-5, this issue.

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This article has been contributed to by US Government employees and their work is in the public domain in the USA.

The findings and conclusions in this article are those of the authors and do not necessarily represent the official positions of the author's agencies (the Centers for Disease Control and Prevention, the National Cancer Institute, the American Cancer Society, or the North American Association of Central Cancer Registries).

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(NAACCR) have collaborated to develop the *Annual Report to the Nation on the Status of Cancer*.¹⁻¹⁷ These reports provide annual updates on cancer incidence, deaths, and trends of the most common cancers in the United States. In addition, each publication features an in-depth analysis of a selected special topic. This year's report provides a detailed analysis of the incidence of liver and intrahepatic bile duct (liver) cancers and rates of liver cancer and hepatitis C virus (HCV) infection-associated deaths.

Worldwide, liver cancer is the fifth most common cancer among men, the ninth most common cancer among women, and the second most common cause of cancer death for men and women combined.¹⁸ Although liver cancer occurs more frequently in less developed regions of the world,¹⁸ it is still a significant health outcome in the United States. In 2012, a total of 28,012 persons in the United States (excluding Nevada) were diagnosed with liver cancer (20,207 men and 7805 women), and 22,972 died of this disease (15,563 men and 7409 women).¹⁹ The relative 5-year survival rate for liver cancer is 16.6% (95% confidence interval [CI], 16.3%-16.9%).¹⁹ Forty-three percent of patients with liver cancer are diagnosed at a localized stage, for which the 5-year relative survival rate is 30.5%.²⁰ Those diagnosed at a regional stage (27%) and a distant stage (18%) have 5-year relative survival rates of 10.7% and 3.1%, respectively.²⁰

Viral hepatitis is an important cause of hepatocellular carcinoma (HCC), the most common histologic type of liver cancer. Chronic infections with hepatitis B virus (HBV) or HCV are well documented risk factors for HCC. Globally, it is reported that both infections contribute to greater than 60% of HCC cases.²¹ In the United States, it has also been reported that chronic HBV and HCV infections are major risk factors for HCC and are correlated with increasing trends in HCC incidence.^{22,23} Data from national US surveys indicate that from 850,000 to 2.2 million persons are living with chronic HBV infection,^{24,25} and from 2.7 to 3.5 million persons are living with chronic HCV infection.^{26,27} The age-specific prevalence of HCV infection also suggests that persons born during 1945 through 1965 are more likely than other birth cohorts to be diagnosed with HCV infection.²⁸ In the absence of improved testing and appropriate treatment, HCV infections among this generation will continue to account for a substantial proportion of deaths from liver cancer.²⁹ Consequently, the CDC and the United States Preventive Services Task Force (USPSTF) recently recommended a 1-time HCV test for persons born during 1945 through 1965.^{30,31} Other

important risk factors for liver cancer include excessive alcohol consumption, obesity, nonalcoholic fatty liver disease, rare metabolic disorders, and type 2 diabetes mellitus.³² In this report, we closely examine incidence and mortality trends from liver cancer among different groups, discuss the potential risk factors contributing to changes in liver cancer rates, and present ongoing public health interventions aimed at reducing the burden of liver cancer in the United States.

MATERIALS AND METHODS

Data Sources, Codes, and Selection Criteria Cancer incidence data

Population-based cancer incidence data were obtained from registries that participate in the CDC's National Program of Cancer Registries (NPCR) and/or the NCI's Surveillance, Epidemiology, and End Results (SEER) program and voluntarily submit their data to NAACCR. Participating registries met NAACCR's data-quality criteria for the December 2014 submission cycle.³³ Site and histology were coded according to the International Classification of Diseases for Oncology (ICD-O) edition in use at the time of diagnosis, converted to the third edition coding,³⁴ and categorized according to SEER site groups.²⁰ Only cases defined as malignant under ICD-O-2 and ICD-O-3 were included in this report.

Incidence rates were calculated for all sites combined, for childhood cancers (ages 0-14 and 0-19 years), and for the most common cancers for each of the 5 major racial and ethnic groups (white, black, Asian and Pacific Islander [API], American Indian/Alaska Native [AI/AN], and Hispanic). Rates for Hispanic ethnicity included individuals from all races identified as Hispanic, except in the special section, as noted. Rates for AI/ANs were based on cases and deaths occurring in counties covered by the Indian Health Service Contract Health Service Delivery Areas (CHSDA), because it has been demonstrated that these areas have more accurate classification of AI/AN race.^{10,35,36}

Cancer incidence data were not available uniformly for every calendar year, geographic area, or racial and ethnic group in the United States. Long-term (1992-2012) incidence trends for all racial and ethnic groups combined were estimated by using data from the SEER-13 registries, which cover approximately 14% of the US population.³⁷ Five-year (2008-2012) average annual incidence rates, 5-year (2008-2012) and 10-year (2003-2012) incidence trends for all racial and ethnic groups combined, and 10-year trends for each of the 5 major racial and ethnic populations were calculated by using combined data from the NPCR and SEER registries as submitted to NAACCR.

Together, participating registries cover 97% (for 2008-2012) and 92% (for 2003-2012) of the US population.

Cancer mortality data

Cause of death was based on death certificate information reported to state vital statistics offices and compiled into a national file for the entire United States by the CDC National Center for Health Statistics' (NCHS) National Vital Statistics System.³⁸ The underlying causes of death were selected according to the International Classification of Disease (ICD) codes and rules in use at the time of death (ICD-8 through ICD-10) and categorized according to SEER site groups to maximize comparability between ICD and ICD-O versions.²⁰ Death rates were calculated for all cancer sites combined, for childhood cancers, and the most common cancers among men and women identified by the incidence analysis. We examined long-term (1975-2012) mortality trends for all racial and ethnic groups combined and 5-year (2008-2012) average annual age-adjusted death rates and 10-year (2003-2012) mortality trends for each of the 5 major racial and ethnic groups.

Population data

The population estimates that were used in this report represent a modification of the intercensal and Vintage 2013 annual times series of July 1; and county population estimates by age, sex, race, and Hispanic origin were produced by the US Census Bureau's Population Estimates Program in collaboration with the CDC's NCHS and with support from the NCI.³⁹ The estimates incorporate intercensal (July 1, 2000-2009) and Vintage 2013 (July 1, 2010-2013) bridged, single-race estimates that are derived from the original multiple race categories in the 2000 and 2010 US Censuses (as specified in the 1997 Office of Management and Budget standards for the collection of data about race and ethnicity).⁴⁰ For most states, population estimates as of July 1 of each year were used to calculate incidence rates, which were presumed to reflect the average population of a defined geographic area for a calendar year; however, some adjustments were made to refine these estimates, as has been done in previous reports.^{16,17,39}

Liver and Intrahepatic Bile Duct Cancer-Specific Incidence and Mortality Data

The special analysis for this report included all invasive liver and intrahepatic bile duct (liver) cancer cases (ICD-O-3 site codes C220 and C221, excluding histology codes 9050-9055; 9140; 9590-9989). Analyses in this section were restricted to 4 large, nonoverlapping racial or ethnic

groups with a sufficient number of cases to produce informative results: non-Hispanic (NH) white, NH black, NH API, and Hispanic. Small counts produced unstable rate estimates for the NH AI/AN group and have been excluded from certain analyses.

To help understand differences in liver cancer incidence rates and trends by birth cohort, we conducted age-period-cohort analyses. We grouped liver cancer incidence data from the SEER-13 registries into 5-year age groups (ages 35-39 through 80-84 years) and 5-year calendar periods (1993-1997, 1998-2002, 2003-2007, and 2008-2012), spanning 13 partially overlapping, 10-year birth cohorts (from 1908-1917 [referred to as "1913," the mid-year of birth] through 1968-1977). To analyze age-specific liver cancer incidence rates by period, data from the SEER-13 registries were grouped into 5-year age groups (35-39 through 80-84 and ≥ 85 years) and 5-year periods (1992-1996, 2000-2004, and 2008-2012), which were the beginning, middle, and end of the 20-year span.

To examine the distribution of liver cancer deaths by race and ethnicity, SEER-18 incidence-based mortality data for liver cancer deaths (ICD-10 codes C22) during 2008 through 2012 were analyzed. All patients in this analysis were diagnosed with and subsequently died of liver cancer, lessening the misclassification of death from liver cancer metastasis as death from primary liver cancer. Patients who had death certificate and autopsy-only diagnoses were excluded. SEER-18 registries cover 28% of the US population.

Because HCV infection is a major contributing factor for HCC in the United States, we also examined HCV and liver cancer-associated mortality for 1999 through 2013. The cancer mortality data and population files used in this analysis were consistent with the files used for other cancer mortality estimates in this report. The data were analyzed to describe mortality by birth year category and year of death and by birth year category and age at death for decedents aged ≥ 35 years who had both HCV and liver cancer listed among causes of death. Birth year and cohort were assigned by subtracting the age at death from the year of death. The underlying cause of death and multiple causes of death were selected according to ICD-10 codes⁴¹ and selection rules in use at the time of death.⁴² HCV and liver cancer-associated deaths were defined as having HCV (ICD-10 codes B17.1 or B18.2) and liver cancer (ICD-10 codes C22.0-C22.9) listed together anywhere on the death record as either the underlying cause or among the multiple causes of death.

TABLE 1. Surveillance, Epidemiology, and End Results (SEER) Cancer Incidence Rate Trends With Joinpoint Analyses From 1992 to 2012 for the Most Common Cancers, by Sex, for All Racial and Ethnic Groups Combined^a

Sex/Cancer Site or Type	Joinpoint Analyses (1992-2012) ^b													
	Trend 1			Trend 2			Trend 3			Trend 4			AAPC ^c	
	Years	APC ^d	Years	APC ^d	Years	APC ^d	Years	APC ^d	Years	APC ^d	2003-2012	2008-2012		
All sites ^e														
Both sexes														
(Delay-adjusted)	1992-1994	-3.1 ^f	1994-1998	0.4	1998-2009	-0.4 ^f	2009-2012	-2.3 ^f	2009-2012	2009-2012	-1.0 ^g	2008-2012	-1.8 ^g	
Men	1992-1994	-3.1 ^f	1994-1998	0.4	1998-2009	-0.3 ^f	2009-2012	-1.5 ^f	2009-2012	2009-2012	-0.7 ^g	2008-2012	-1.2 ^g	
(Delay-adjusted)	1992-1994	-5.7 ^f	1994-2009	-0.5 ^f	2009-2012	-4.1 ^f	2009-2012	-3.1 ^f	2009-2012	2009-2012	-1.7 ^g	2008-2012	-3.2 ^g	
Women	1992-1998	0.7 ^f	1998-2012	-0.3 ^f	2003-2012	0.0	2003-2012	0.0	2003-2012	2003-2012	-0.3 ^g	2008-2012	-2.5 ^g	
(Delay-adjusted)	1992-1998	0.8 ^f	1998-2003	-0.6	2003-2012	0.0	2003-2012	0.0	2003-2012	2003-2012	0.0	2008-2012	-0.3 ^g	
Children (ages 0-14 years)	1992-2012	0.7 ^f									0.0	2008-2012	0.0	
(Delay-adjusted)	1992-2012	0.8 ^f									0.7 ^g	2008-2012	0.7 ^g	
Children (ages 0-19 years)	1992-2012	0.7 ^f									0.8 ^g	2008-2012	0.8 ^g	
(Delay-adjusted)	1992-2012	0.8 ^f									0.7 ^g	2008-2012	0.7 ^g	
Top 17 cancers among men ^h														
Prostate	1992-1995	-11.1 ^f	1995-2000	2.1	2000-2010	-2.0 ^f	2010-2012	-12.4 ^f	2010-2012	2010-2012	-4.4 ^g	2008-2012	-7.3 ^g	
(Delay-adjusted)	1992-1995	-11.1 ^f	1995-2000	2.1	2000-2010	-1.8 ^f	2010-2012	-11.2 ^f	2010-2012	2010-2012	-4.0 ^g	2008-2012	-6.6 ^g	
Lung and bronchus	1992-2009	-1.9 ^f	2009-2012	-4.2 ^f	2009-2012	-3.3 ^f	2009-2012	-3.0 ^f	2009-2012	2009-2012	-2.7 ^g	2008-2012	-3.6 ^g	
(Delay-adjusted)	1992-2009	-1.9 ^f	2009-2012	-3.3 ^f	2009-2012	-3.3 ^f	2009-2012	-3.0 ^f	2009-2012	2009-2012	-2.4 ^g	2008-2012	-3.0 ^g	
Colon and rectum	1992-1995	-2.6 ^f	1995-1998	1.4	1998-2008	-2.5 ^f	2008-2012	-4.0 ^f	2008-2012	2008-2012	-3.2 ^g	2008-2012	-4.0 ^g	
(Delay-adjusted)	1992-1995	-2.6 ^f	1995-1998	1.4	1998-2008	-2.5 ^f	2008-2012	-3.6 ^f	2008-2012	2008-2012	-3.0 ^g	2008-2012	-3.6 ^g	
Urinary bladder	1992-2007	0.1	2007-2012	-1.7 ^f	2007-2012	-1.7 ^f	2007-2012	-1.7 ^f	2007-2012	2007-2012	-0.9 ^g	2008-2012	-1.7 ^g	
(Delay-adjusted)	1992-2007	0.1	2007-2012	-1.2 ^f	2007-2012	-1.2 ^f	2007-2012	-1.2 ^f	2007-2012	2007-2012	-0.6 ^g	2008-2012	-1.2 ^g	
Melanoma of the skin	1992-2008	2.6 ^f	2008-2012	-0.4	2008-2012	-0.4	2008-2012	-0.4	2008-2012	2008-2012	1.2 ^g	2008-2012	-0.4	
(Delay-adjusted)	1992-1996	5.0 ^f	1996-2012	2.0 ^f	1996-2012	2.0 ^f	1996-2012	2.0 ^f	1996-2012	2008-2012	2.0 ^g	2008-2012	2.0 ^g	
Non-Hodgkin lymphoma	1992-1995	2.8	1995-1998	-2.1	1998-2010	0.6 ^f	2010-2012	-4.1	2010-2012	2010-2012	-0.5	2008-2012	-1.8	
(Delay-adjusted)	1992-1995	2.8	1995-1998	-2.1	1998-2010	0.7 ^f	2010-2012	-2.8	2010-2012	2010-2012	0.5	2008-2012	-1.1	
Kidney and renal pelvis	1992-2004	1.9 ^f	2004-2008	4.4 ^f	2008-2012	-1.4	2008-2012	-2.8	2008-2012	2008-2012	1.5 ^g	2008-2012	-1.4	
(Delay-adjusted)	1992-1999	1.1 ^f	1999-2008	3.2 ^f	2008-2012	-0.1	2008-2012	-0.1	2008-2012	2008-2012	1.7 ^g	2008-2012	-0.1	
Oral cavity and pharynx	1992-2001	-1.8 ^f	2001-2012	0.2	2003-2012	0.8 ^f	2003-2012	0.8 ^f	2003-2012	2003-2012	0.2	2008-2012	0.2	
(Delay-adjusted)	1992-2003	-1.5 ^f	2003-2012	0.8 ^f	2003-2012	0.8 ^f	2003-2012	0.8 ^f	2003-2012	2003-2012	0.1	2008-2012	0.8 ^g	
Leukemia	1992-2012	0.1	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	2006-2012	0.1	2007-2012	0.8 ^g	
(Delay-adjusted)	1992-2006	0.2	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	2006-2012	0.1	2007-2012	1.8 ^g	
Pancreas	1992-2003	0.0	2003-2006	2.9	2006-2012	0.1	2006-2012	0.1	2006-2012	2006-2012	1.0	2007-2012	1.0	
(Delay-adjusted)	1992-2001	0.0	2001-2012	1.2 ^f	2001-2012	1.2 ^f	2001-2012	1.2 ^f	2001-2012	2001-2012	1.2 ^g	2007-2012	1.2 ^g	
Liver and intrahepatic bile duct	1992-1999	4.6 ^f	1999-2002	0.5	2002-2007	5.4 ^f	2002-2007	1.8 ^f	2002-2007	2002-2007	3.4 ^g	2007-2012	1.8 ^g	
(Delay-adjusted)	1992-2012	3.7 ^f	1999-2002	0.5	2002-2007	5.4 ^f	2002-2007	1.8 ^f	2002-2007	2002-2007	3.7 ^g	2007-2012	3.7 ^g	
Stomach	1992-2012	-1.7 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	2006-2012	3.7 ^g	2007-2012	3.7 ^g	
(Delay-adjusted)	1992-2012	-1.7 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	2006-2012	3.7 ^g	2007-2012	3.7 ^g	
Esophagus	1992-2012	-0.2	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	2006-2012	3.7 ^g	2007-2012	3.7 ^g	
(Delay-adjusted)	1992-2012	-0.2	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	2006-2012	3.7 ^g	2007-2012	3.7 ^g	
Brain and other nervous system	1992-2012	-0.3 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	2006-2012	3.7 ^g	2007-2012	3.7 ^g	
(Delay-adjusted)	1992-2012	-0.2 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	1.8 ^f	2006-2012	2006-2012	3.7 ^g	2007-2012	3.7 ^g	
Myeloma	1992-2012	0.7 ^f	2006-2012	3.0 ^f	2006-2012	3.0 ^f	2006-2012	3.0 ^f	2006-2012	2006-2012	3.0 ^g	2007-2012	3.0 ^g	
(Delay-adjusted)	1992-2006	0.4	2006-2012	3.0 ^f	2006-2012	3.0 ^f	2006-2012	3.0 ^f	2006-2012	2006-2012	3.0 ^g	2007-2012	3.0 ^g	
Thyroid	1992-1995	-3.0	1995-2012	5.2 ^f	1995-2012	5.2 ^f	1995-2012	5.2 ^f	1995-2012	2006-2012	5.2 ^g	2007-2012	5.2 ^g	
(Delay-adjusted)	1992-1995	-3.2	1995-2012	5.3 ^f	1995-2012	5.3 ^f	1995-2012	5.3 ^f	1995-2012	2006-2012	5.2 ^g	2007-2012	5.2 ^g	
Larynx	1992-2003	-3.1 ^f	2003-2012	-1.9 ^f	2003-2012	-1.9 ^f	2003-2012	-1.9 ^f	2003-2012	2003-2012	5.3 ^g	2007-2012	5.3 ^g	
(Delay-adjusted)	1992-2003	-3.2 ^f	2003-2012	-1.7 ^f	2003-2012	-1.7 ^f	2003-2012	-1.7 ^f	2003-2012	2003-2012	5.3 ^g	2007-2012	5.3 ^g	
Top 18 cancers among women ^h														
Breast	1992-1999	1.3 ^f	1999-2004	-2.2 ^f	2004-2012	0.2	2004-2012	0.2	2004-2012	2004-2012	-0.1	2008-2012	0.2	
(Delay-adjusted)	1992-1999	1.3 ^f	1999-2004	-2.2 ^f	2004-2012	0.3	2004-2012	0.3	2004-2012	2004-2012	0.0	2008-2012	0.3	
Lung and bronchus	1992-2007	0.0	2007-2012	-2.4 ^f	2007-2012	-2.4 ^f	2007-2012	-2.4 ^f	2007-2012	2007-2012	-1.3 ^g	2008-2012	-2.4 ^g	
(Delay-adjusted)	1992-2007	0.0	2007-2012	-1.9 ^f	2007-2012	-1.9 ^f	2007-2012	-1.9 ^f	2007-2012	2007-2012	-1.1 ^g	2008-2012	-1.9 ^g	

TABLE 1. Continued

Sex/Cancer Site or Type	Joinpoint Analyses (1992-2012) ^b												
	Trend 1			Trend 2			Trend 3			Trend 4			
	Years	APC ^d	APC ^d	Years	APC ^d	APC ^d	Years	APC ^d	APC ^d	Years	APC ^d	APC ^d	
Colon and rectum (Delay-adjusted)	1992-1995	-1.8 ^f	1.8	1995-1998	1.8	1998-2008	-2.0 ^f	2008-2012	-4.1 ^f	2008-2012	-2.9 ^g	2008-2012	-4.1 ^h
Corpus and uterus, NOS (Delay-adjusted)	1992-1995	-1.8 ^f	1.8	1995-1998	1.8	1998-2008	-2.0 ^f	2008-2012	-3.8 ^f	2008-2012	-2.8 ^g	2008-2012	-3.8 ^h
Thyroid (Delay-adjusted)	1992-2006	-0.1	-0.8	1997-2004	-0.8	2004-2012	1.8 ^f				1.5 ^g		1.8 ^h
Non-Hodgkin lymphoma (Delay-adjusted)	1992-1999	4.1 ^f	2.3 ^f	2006-2012	2.3 ^f	2009-2012	1.4	2009-2012	1.4	2009-2012	5.0 ^g	2009-2012	2.3 ^h
Melanoma of the skin (Delay-adjusted)	1992-2004	1.3 ^f	6.9 ^f	1999-2009	6.9 ^f	2004-2012	1.8	2009-2012	1.8	2009-2012	5.2 ^g	2009-2012	3.0 ^h
Ovary ^e (Delay-adjusted)	1992-2004	1.3 ^f	-0.8 ^f	2004-2012	-0.8 ^f	2010-2012	-3.1				-0.5		-0.8 ^h
Kidney and renal pelvis (Delay-adjusted)	1992-1997	4.0 ^f	0.5	1997-2010	1.6 ^f	2005-2012	0.5				0.5		0.5
Pancreas (Delay-adjusted)	1992-2005	2.4 ^f	3.1 ^f	1998-2008	3.1 ^f	2008-2012	3.1 ^f	2008-2012	-1.3	2008-2012	1.2 ^g	2008-2012	-1.3
Leukemia (Delay-adjusted)	1992-2012	-0.9 ^f	3.6 ^f	2000-2007	3.6 ^f	1999-2012	1.1 ^f	2007-2012	-0.1		1.5 ^g		-0.1
Urinary bladder (Delay-adjusted)	1992-2004	-0.2	-1.2 ^f	2004-2012	-1.2 ^f						1.1 ^g		1.1 ^h
Cervix uteri (Delay-adjusted)	1992-2012	-2.4 ^f	-1.1 ^f	2004-2012	-1.1 ^f						0.3 ^g		0.3 ^h
Oral cavity and pharynx (Delay-adjusted)	1992-2012	-0.7 ^f	0.5	2005-2012	0.5						0.7 ^g		0.7 ^h
Brain and other nervous system (Delay-adjusted)	1992-2005	-1.1 ^f	-0.2								0.7 ^g		0.7 ^h
Myeloma (Delay-adjusted)	1992-2012	0.0	-0.2								-1.1 ^g		-1.2 ^h
Stomach (Delay-adjusted)	1992-2012	0.7 ^f	-0.7 ^f								-1.0 ^g		-1.1 ^h
Liver and intrahepatic bile duct (Delay-adjusted)	1992-1996	6.9 ^f	2.4 ^f	1996-2012	2.4 ^f						-2.4 ^g		-2.4 ^h
	1992-2012	3.0 ^f	3.0 ^f								-0.7 ^g		-0.7 ^h

Abbreviations: AAPC, average annual percent change; APC, annual percent change; NOS, not otherwise specified.
^a Source: Surveillance, Epidemiology, and End Results (SEER)-13 areas covering about 14% of the US population (Connecticut, Hawaii, Iowa, Utah, and New Mexico; the Alaska Native Tumor Registry, rural Georgia; and the metropolitan areas of San Francisco, Los Angeles, San Jose-Monterey, Detroit, Atlanta, and Seattle-Puget Sound).
^b Joinpoint analyses with up to 3 joinpoints yielding up to 4 trend segments (Trends 1-4) were based on rates per 100,000 persons and were age-adjusted to the 2000 US standard population (19 age groups; ages <1 year, 1-4 years, 5-9 years, ..., 80-84 years, and ≥85 years; Census publication p25-1130 [US Bureau of the Census, Current Population Reports, p25-1130, Washington, DC: US Government Printing Office; 2000]). For joinpoint analysis, the Joinpoint Regression Program was used (version 4.2.0.0, April 2015; Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD).
^c The AAPC is a weighted average of the APCs calculated by joinpoint regression.
^d The APC is based on rates that were age-adjusted to the 2000 US standard population (19 age groups; Census publication p25-1130).
^e All sites exclude myelodysplastic syndromes and borderline tumors; ovary excludes borderline tumors.
^f The APC is statistically significantly different from zero (2-sided t test; $P < .05$).
^g The AAPC is statistically significantly different from zero (2-sided Z test; $P < .05$).
^h Cancers are listed in descending rank order of sex-specific, age-adjusted incidence rates for 2008 through 2012 for all racial and ethnic groups combined (using data from the National Program of Cancer Registries [NPCR] and SEER Program areas reported by the North American Association of Central Cancer Registries [NAACCR]) as meeting high-quality incidence data standards for 2008-2012. More than 15 cancers may appear under men and women to include the top 15 cancers in each racial and ethnic group.

Statistical Methods

Incidence and death rates and trends

Age-adjusted rates were expressed per 100,000 persons on the basis of the 2000 US Standard Population and were generated by using SEER*Stat software, version 8.2.1.⁴³ Corresponding 95% CIs were calculated as modified γ intervals.⁴⁴ For stability and reliability, incidence rates were suppressed if there were fewer than 16 cases for the time interval, and incidence trends were suppressed if there were fewer than 10 cases for at least a year within the time interval. Death rates were suppressed if there were fewer than 10 deaths.

Trends in age-adjusted cancer incidence and death rates were estimated using joinpoint regression.^{45,46} Up to 5 joinpoints were allowed in models for 1975 to 2012, up to 3 joinpoints were allowed in models for 1992 to 2012, and up to 2 joinpoints were allowed in models for 2003 to 2012. The resulting trends were described according to the annual percent change (APC). The average APC (AAPC) was estimated as a weighted geometric average of the APCs, with the weights equal to the length of each line segment during the prespecified, fixed interval.⁴⁷ Long-term incidence trends were calculated by using both observed and delay-adjusted SEER-13 data.⁴⁸ Descriptions of the long-term incidence trends were based on the delay-adjusted data unless otherwise noted. Delay-adjustment factors are not currently published for NPCR; thus, all 5-year and 10-year trends were based on observed NPCR and SEER combined data without delay adjustment. We used the t test and the Z test, respectively, to test whether the APC and AAPC were statistically different from zero. All statistical tests were 2-sided. In describing trends, the term *increase* or *decrease* was used when the slope of the trend (APC or AAPC) was statistically significant (2-sided $P < .05$). For nonstatistically significant trends, terms such as *stable*, *nonsignificant increase*, and *nonsignificant decrease* were used.

Liver Cancer Age-Period-Cohort and Estimated Years-of-Life-Lost Analysis

Liver cancer incidence rates were examined by sex, age, race or ethnicity, state, and year of diagnosis by using the same methods described above. The NCI's online age-period-cohort analysis tool was used to calculate cohort rate ratios, comparing liver cancer incidence rates in each birth cohort relative to the 1943 birth cohort, and adjusting for age and period effects.⁴⁹ The 1943 birth cohort was selected as the reference because it immediately preceded the known increase in the prevalence of HCV infection for individuals born during 1945 through 1965.²⁸

Proportions of incidence-based deaths from liver cancer and median age at death were determined by sex and race or ethnicity.⁵⁰ Person-years of life lost (PYLL) to liver cancer were calculated by linking the "expectation of life at age x " column of the US 2010 complete life tables to single-year age-at-death data.^{20,51,52} All-race life tables were used to calculate overall PYLL, whereas single-sex, all-race tables were used for gender-specific analyses. The average PYLL (APYLL) per death was calculated as the PYLL divided by the number of deaths.

HCV and liver cancer-associated death rates during 1999 through 2013 for those aged ≥ 35 years according to 3 birth-year categories (those born before 1945, during 1945-1965, and during 1966-1978) were examined by year at death. To remove the effect of age, HCV and liver cancer-associated death rates also were examined using slightly more refined birth-year categories (those born before 1945, during 1945-1949, during 1950-1959, during 1960-1965, and during 1966-1978) and by age at death. Crude HCV and liver cancer-associated death rates were calculated by dividing the number of deaths in each category by the US Census population estimate for each year. A similar methodology was applied in a previous study that examined the burden of mortality associated with viral hepatitis in the United States from 1999 to 2007.⁵³

RESULTS

Long-Term Trends of Cancer Incidence Rates for the Most Common Cancers

Trends in delay-adjusted cancer incidence rates using data from SEER-13 registries that submitted data to the NCI from 1992 to 2012 are presented in Table 1. Cancer incidence rates decreased among men during each period, but at different rates. In contrast, cancer incidence rates among women increased slightly (0.8% per year) from 1992 to 1998, then remained stable. Among children in both age groups, (ages 0-14 and 0-19 years), incidence rates increased from 1992 to 2012 with an APC of 0.8%.

During 2003 through 2012, the AAPC indicated that overall cancer incidence rates for all persons combined decreased on average 0.7% per year (Table 1). Among men, overall cancer incidence decreased on average by 1.4% per year during 2003 through 2012; however, among women, rates were stable during this 10-year period. Among men, incidence rates for 7 of the 17 most common cancers decreased from 2003 to 2012 (prostate, colon and rectum [colorectal], lung and bronchus [lung], stomach, larynx, urinary bladder [bladder], and brain and other nervous system [brain]). The most striking decline

was for prostate cancer, which had an average 6.6% decline per year for the most recent 5-year period (2008-2012). In contrast, incidence rates increased among men during 2003 through 2012 for 8 cancers (thyroid, liver, myeloma, melanoma of the skin [melanoma], kidney and renal pelvis [kidney], leukemia, pancreas, and oral cavity and pharynx). Among women, incidence rates for 6 of the 18 most common cancers decreased during 2003 through 2012 (colorectal, cervix uteri [cervix], lung, bladder, ovary, and stomach), whereas incidence rates among women increased during 2003 through 2012 for 8 cancers (thyroid; liver; corpus and uterus, not otherwise specified [uterus]; kidney; pancreas; melanoma; leukemia; and myeloma). Incidence rates were stable for all other sites.

Long-Term Trends of Cancer Death Rates for the Most Common Cancers

The long-term (1975-2012) mortality trend analysis revealed that the overall cancer death rate in the United States has generally declined since the early 1990s for adults and since the 1970s for children (Table 2). More recently, from 2003 to 2012, death rates continued to decline by an average of 1.5% per year overall, by 1.3% per year for children ages 0 to 14 years, and by 2.0% per year for children ages 0 to 19 years. Among men, death rates declined overall from 2003 to 2012 (1.8% per year). Relatively large declines among men were also observed for cancers of the prostate (3.5% per year), stomach (3.3% per year), colorectum (2.9% per year), lung (2.7% per year), and larynx (2.5% per year) and for non-Hodgkin lymphoma (2.2% per year). Declines in death rates during this time among men were $\leq 1\%$ per year for leukemia, myeloma, and cancers of the esophagus and kidney. Death rates among men remained stable during this time for melanoma and for cancers of the bladder, brain, and oral cavity and pharynx. Death rates increased among men during 2003 through 2012 for cancers of the liver (2.8% per year); soft tissue, including the heart (1.1% per year); and pancreas (0.3% per year).

Among women, during 2003 through 2012, death rates declined overall (1.4% per year) and for non-Hodgkin lymphoma (3.1% per year), colorectal cancer (2.9% per year), leukemia (1.2% per year), and myeloma (1.2% per year), and for cancers of the stomach (2.6% per year), ovary (2.0% per year), breast (1.9% per year), lung (1.4% per year), oral cavity and pharynx (1.3% per year), gallbladder (1.2% per year), kidney (1.0% per year), cervix (0.9% per year), and bladder (0.4% per year), and remained stable for brain cancer, but increased for cancers

of the liver (2.2% per year), uterus (1.1% per year), and pancreas (0.4% per year).

Current Cancer Incidence Rates and Trends by Race and Ethnicity

By using data from both SEER and NPCR registries, 5-year (2008-2012) average annual incidence rates and 5-year (2008-2012) and 10-year (2003-2012) incidence trends were analyzed by site, sex, and race and ethnicity (Table 3). During 2008 through 2012, observed rates of all cancers combined in all racial groups were lower among women than among men (412.6 vs 512.7 per 100,000). Black men had the highest overall cancer incidence rate (573.6 per 100,000) of any racial or ethnic group, and non-Hispanics had higher rates than Hispanics (464.7 vs 353.7 per 100,000). Among women, white women had the highest overall cancer incidence rate during this time of any racial or ethnic group (418.4 per 100,000). Prostate cancer remained the most common cancer among men in each racial and ethnic group, and the rates were substantially higher than for any other type of cancer. Lung and colorectal cancer were the second and third most common cancers, respectively, among men of all racial and ethnic groups, except among Hispanic men, in whom these ranks were reversed. Breast cancer was the most common cancer among women of all racial and ethnic groups. Like in men, lung cancer was the second most common cancer among women, followed by colorectal cancer, except among API and Hispanic women, in whom the ranks were reversed. Rankings of other cancers for both men and women varied by race and ethnicity. White children had higher cancer incidence rates than children of other racial and ethnic groups.

Overall cancer incidence rates among men declined in each racial and ethnic group during 2003 through 2012. During 2003 through 2012, the incidence rates for the 4 most common cancers among men decreased (prostate, lung, colorectal, and bladder) for all races except among black men, for whom bladder cancer incidence rates remained stable. Thyroid cancer incidence rates among men increased $>5\%$ annually during 2003 through 2012 for all racial and ethnic groups except for AI/AN, for whom the increase was not statistically significant. Trends in incidence rates for most cancers among men in each racial and ethnic group were similar in direction to those of all men combined, but some trends were not statistically significant. Oral cancer incidence rates decreased among black men (-2.5% per year), and liver cancer incidence rates decreased among API (-1.3% per

TABLE 2. US Cancer Death Rate Trends With Joinpoint Analyses From 1975 to 2012 for the Most Common Cancers, by Sex, for All Racial and Ethnic Groups Combined^a

Sex/Cancer Site or Type	Joinpoint Analyses (1975-2012) ^b													
	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		Trend 6		AAPC ^c	
	Years	APC ^d	Years	APC ^d	Years	APC ^d	Years	APC ^d	Years	APC ^d	Years	APC ^d	2003-2012	2008-2012
All sites														
Both sexes	1975-1984	0.5 ^e	1984-1991	0.3 ^e	1991-1994	-0.5	1994-1998	-1.3 ^e	1998-2001	-0.8	2001-2012	-1.5 ^e	-1.5 ^f	-1.5 ^f
Men	1975-1979	1.0 ^e	1979-1990	0.3 ^e	1990-1993	-0.5	1993-2001	-1.5 ^e	2001-2012	-1.8 ^e			-1.8 ^f	-1.8 ^f
Women	1975-1990	0.6 ^e	1990-1994	-0.2	1994-2002	-0.8 ^e	2002-2012	-1.4 ^e					-1.4 ^f	-1.4 ^f
Children (ages 0-14 years)	1975-1996	-2.9 ^e	1996-2012	-1.3 ^e									-1.3 ^f	-1.3 ^f
Children (ages 0-19 years)	1975-1998	-2.7 ^e	1998-2002	0.0	2002-2012	-2.0 ^e							-2.0 ^f	-2.0 ^f
Top 17 cancers among men^g														
Lung and bronchus	1975-1978	2.5 ^e	1978-1984	1.2 ^e	1984-1990	0.4 ^e	1990-1993	-1.1	1993-2005	-1.9 ^e	2005-2012	-2.9 ^e	-2.7 ^f	-2.9 ^f
Prostate	1975-1987	0.9 ^e	1987-1991	3.0 ^e	1991-1994	-0.5	1994-1998	-4.2 ^e	1998-2012	-3.5 ^e			-3.5 ^f	-3.5 ^f
Colon and rectum	1975-1978	0.8	1978-1984	-0.3	1984-1990	-1.3 ^e	1990-2002	-2.0 ^e	2002-2005	-3.9 ^e	2005-2012	-2.6 ^e	-2.9 ^f	-2.6 ^f
Pancreas	1975-1986	-0.8 ^e	1986-2000	-0.3 ^e	2000-2012	0.3 ^e							0.3 ^f	0.3 ^f
Leukemia	1975-1980	0.5	1980-1987	-0.7 ^e	1987-1995	0.1	1995-2012	-0.9 ^e					-0.9 ^f	-0.9 ^f
Liver and intrahepatic bile duct	1975-1979	0.3	1979-1987	2.3 ^e	1987-1996	3.9 ^e	1996-1999	0.6	1999-2007	2.4 ^e	2007-2012	3.1 ^e	2.8 ^f	3.1 ^f
Non-Hodgkin lymphoma	1975-1991	2.7 ^e	1991-1997	1.6 ^e	1997-2006	-2.9 ^e	2006-2012	-1.9 ^e					-2.2 ^f	-1.9 ^f
Urinary bladder	1975-1983	-1.4 ^e	1983-1987	-2.8 ^e	1987-1993	0.2	1993-1997	-1.1	1997-2012	0.0			0.0	0.0
Esophagus	1975-1985	0.7 ^e	1985-1994	1.2 ^e	1994-2005	0.4 ^e	2005-2012	-1.0 ^e					-0.7 ^f	-1.0 ^f
Kidney and renal pelvis	1975-1991	1.1 ^e	1991-2001	-0.1	2001-2012	-0.8 ^e							-0.8 ^f	-0.8 ^f
Brain and other nervous system	1975-1977	4.4	1977-1982	-0.4	1982-1991	1.3 ^e	1991-2007	-1.0 ^e	2007-2012	0.7			0.0	0.7
Stomach	1975-1987	-2.4 ^e	1987-1990	-0.4	1990-2012	-3.3 ^e							-3.3 ^f	-3.3 ^f
Myeloma	1975-1994	1.5 ^e	1994-2012	-1.0 ^e									-1.0 ^f	-1.0 ^f
Melanoma of the skin	1975-1990	2.2 ^e	1990-2002	0.0	2002-2009	1.0 ^e	2009-2012	-1.6					0.1	-0.9
Oral cavity and pharynx	1975-1977	0.7	1977-1993	-2.0 ^e	1993-2000	-2.9 ^e	2000-2009	-1.3 ^e	2009-2012	1.7			-0.3	1.0
Larynx	1975-1994	-0.8 ^e	1994-2012	-2.5 ^e									-2.5 ^f	-2.5 ^f
Soft tissue including heart	1975-1980	7.6 ^e	1980-1997	1.2 ^e	1997-2002	-3.4 ^e	2002-2012	1.1 ^e					1.1 ^f	1.1 ^f

TABLE 2. Continued

Sex/Cancer Site or Type	Joinpoint Analyses (1975-2012) ^b													
	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		Trend 6		AAPC ^c	
	Years	APC ^d	Years	APC ^d	Years	APC ^d	Years	APC ^d	Years	APC ^d	Years	APC ^d	2003-2012	2008-2012
Top 17 cancers among women ⁹														
Lung and bronchus	1975-1982	6.0 ^e	1982-1990	4.2 ^e	1990-1995	1.7 ^e	1995-2003	0.3 ^e	2003-2007	-0.8	2007-2012	-1.9 ^e	-1.4 ^f	-1.9 ^f
Breast	1975-1990	0.4 ^e	1990-1995	-1.8 ^e	1995-1998	-3.3 ^e	1998-2012	-1.9 ^e					-1.9 ^f	-1.9 ^f
Colon and rectum	1975-1984	-1.0 ^e	1984-2001	-1.8 ^e	2001-2012	-2.9 ^e							-2.9 ^f	-2.9 ^f
Pancreas	1975-1984	0.8 ^e	1984-2000	0.1	2000-2012	0.4 ^e							0.4 ^f	0.4 ^f
Ovary	1975-1982	-1.2 ^e	1982-1992	0.4 ^e	1992-1998	-1.2 ^e	1998-2002	1.1	2002-2012	-2.0 ^e			-2.0 ^f	-2.0 ^f
Leukemia	1975-1980	0.7	1980-1999	-0.4 ^e	1999-2012	-1.2 ^e							-1.2 ^f	-1.2 ^f
Non-Hodgkin lymphoma	1975-1994	2.2 ^e	1994-1997	0.8	1997-2012	-3.1 ^e							-3.1 ^f	-3.1 ^f
Corpus and uterus, NOS	1975-1989	-1.6 ^e	1989-1997	-0.7 ^e	1997-2009	0.3 ^e	2009-2012	2.5 ^e					1.1 ^f	2.0 ^f
Liver and intrahepatic bile duct	1975-1978	-1.5	1978-1988	1.4 ^e	1988-1995	3.9 ^e	1995-2000	0.4	2000-2008	1.4 ^e	2008-2012	3.1 ^e	2.2 ^f	3.1 ^f
Brain and other nervous system	1975-1992	1.0 ^e	1992-2006	-1.1 ^e	2006-2012	0.1							-0.3	0.1
Myeloma	1975-1993	1.5 ^e	1993-2002	-0.5	2002-2009	-2.7 ^e	2009-2012	2.0					-1.2 ^f	0.8
Kidney and renal pelvis	1975-1995	1.1 ^e	1995-2012	-1.0 ^e									-1.0 ^f	-1.0 ^f
Stomach	1975-1987	-2.8 ^e	1987-1990	-0.4	1990-2012	-2.6 ^e							-2.6 ^f	-2.6 ^f
Cervix uteri	1975-1982	-4.3 ^e	1982-1996	-1.6 ^e	1996-2003	-3.8 ^e	2003-2012	-0.9 ^e					-0.9 ^f	-0.9 ^f
Urinary bladder	1975-1986	-1.7 ^e	1986-2012	-0.4 ^e									-0.4 ^f	-0.4 ^f
Oral cavity and pharynx	1975-1990	-0.9 ^e	1990-2005	-2.4 ^e	2005-2012	-1.0 ^e							-1.3 ^f	-1.0 ^f
Gallbladder	1975-2002	-2.7 ^e	2002-2012	-1.2 ^e									-1.2 ^f	-1.2 ^f

Abbreviations: AAPC, average annual percent change; APC, annual percent change; NOS, not otherwise specified.

^aSource: National Center for Health Statistics public-use data file for the total United States, 1975-2012.

^bJoinpoint analyses with up to 5 joinpoints yielding up to 6 trend segments (Trends 1-6) were based on rates per 100,000 persons and were age-adjusted to the 2000 US standard population (19 age groups; ages <1 year, 1-4 years, 5-9 years, ..., 80-84 years, ≥85 years; Census publication p25-1130 [US Bureau of the Census, Current Population Reports, p25-1130. Washington, DC: US Government Printing Office; 2000]). For joinpoint analysis, the Joinpoint Regression Program was used (version 4.2.0.0, April 2015; Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD).

^cThe AAPC is a weighted average of the APCs calculated by joinpoint regression.

^dThe APC is based on rates that were age-adjusted to the 2000 US standard population (19 age groups; Census publication p25-1130).

^eThe APC is statistically significantly different from zero (2-sided t test; $P < .05$).

^fThe AAPC is statistically significantly different from zero (2-sided Z test; $P < .05$).

⁹Cancers are listed in descending rank order of sex-specific, age-adjusted death rates for 2008 through 2012 for all racial and ethnic groups combined. More than 15 cancers may appear under men and women to include the top 15 cancers in each racial and ethnic group.

TABLE 3. Cancer Incidence Rates for 2008 to 2012 and Fixed-Interval Trends From 2003 to 2012 for the Top Cancers by Sex, Race, and Ethnicity for Areas in the United States With High-Quality Incidence Data^a

Sex/Cancer Site or Type ^c	All Races and Ethnicities																	
	White ^b			Black ^b			API ^b			AI/AN (CHSDA) ^b			Hispanic ^b			Non-Hispanic ^b		
	2003-2012	2008-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	2003-2012	
All sites ^d	454.0	-0.9 ^g	-2.1 ^g	454.5	-0.9 ^g	-1.2 ^g	292.1	-0.9 ^g	385.6	-1.6 ^g	353.7	-1.3 ^g	464.7	-0.8 ^g				
Both sexes	512.7	-1.7 ^g	-3.4 ^g	506.5	-1.6 ^g	-2.2 ^g	309.7	-1.9 ^g	416.2	-2.8 ^g	400.8	-2.4 ^g	524.1	-1.6 ^g				
Men	412.6	-0.3 ^g	-0.8 ^g	418.4	-0.2	-0.2	283.1	0.2	367.2	-0.4	324.7	-0.5 ^g	422.3	-0.2 ^g				
Women	16.0	0.5	0.5	16.6	0.4	0.5	12.8	0.8	11.1	-1.3	15.6	-0.1	16.2	0.6 ^g				
Children (ages 0-14 years)	17.4	0.4 ^g	0.4 ^g	18.2	0.3	0.3	13.8	1.1	12.6	-0.5	16.8	0.3	17.6	0.5 ^g				
Children (ages 0-19 years)																		
Top 17 cancers among men																		
Prostate	1	131.5	-3.2 ^g	121.4	-3.6 ^g	-3.5 ^g	1	67.8	-4.5 ^g	90.5	-5.8 ^g	1	133.5	-3.1 ^g				
Lung and bronchus	2	76.7	-2.5 ^g	76.2	-2.5 ^g	-2.8 ^g	2	47.4	-1.8 ^g	66.2	-2.6 ^g	3	43.3	-3.1 ^g				
Colon and rectum	3	48.3	-3.6 ^g	47.1	-3.8 ^g	-3.5 ^g	3	39.0	-2.6 ^g	50.4	-1.9 ^g	2	44.6	-3.0 ^g				
Urinary bladder	4	36.4	-1.1 ^g	38.6	-1.1 ^g	0.0	6	15.4	-1.0 ^g	18.3	-1.9 ^g	5	20.1	-2.3 ^g				
Melanoma of the skin	5	25.4	1.7 ^g	28.4	1.7 ^g	-1.0	20	1.5	-1.7	6.8	-1.0	17	4.7	-1.3				
Non-Hodgkin lymphoma	6	23.1	-0.7 ^g	23.7	-0.7 ^g	-0.4	5	15.7	0.2	17.0	-2.1	6	19.9	-0.8 ^g				
Kidney and renal pelvis	7	21.5	1.0 ^g	21.6	1.0 ^g	1.6 ^g	9	10.8	1.3	29.7	-1.3	4	20.6	0.6 ^g				
Oral cavity and pharynx	8	16.9	0.6 ^g	17.3	0.9 ^g	-2.5 ^g	8	10.9	0.2	14.7	1.1	11	10.9	-0.5				
Leukemia	9	16.8	-0.3 ^g	17.3	-0.4 ^g	-0.1	11	9.6	0.6	11.2	-2.5	9	12.7	-0.7				
Pancreas	10	14.0	0.8 ^g	13.8	0.9 ^g	0.0	10	9.8	0.1	11.3	-1.1	10	12.0	-0.2				
Liver and intra-hepatic bile duct	11	11.5	3.5 ^g	10.3	3.7 ^g	3.9 ^g	4	20.6	-1.3 ^g	18.7	3.2	7	19.3	1.8 ^g				
Stomach	12	9.3	-1.3 ^g	8.4	-1.1 ^g	-2.3 ^g	7	14.5	-3.8 ^g	12.0	-4.2 ^g	8	13.5	-2.9 ^g				
Esophagus	13	8.3	-1.4 ^g	8.5	-0.9	-5.3 ^g	15	3.8	-2.2	7.2	-0.2	14	5.3	-2.3 ^g				
Brain and other nervous system	14	7.8	-0.7 ^g	8.3	-0.7 ^g	0.0	14	4.4	-0.5	5.3	-0.4	13	5.9	-1.3 ^g				
Myeloma	15	7.7	0.8 ^g	7.1	0.7 ^g	0.5	13	4.5	0.5	6.3	-1.5	12	7.5	0.5				
Thyroid	16	6.8	5.2 ^g	7.3	5.3 ^g	4.6 ^g	12	6.3	6.4 ^g	4.0	2.5	16	5.1	5.2 ^g				
Larynx	17	6.3	-2.8 ^g	6.2	-2.5 ^g	-3.9 ^g	18	2.3	-2.0	5.8	-2.2	15	5.2	-3.7 ^g				
Top 18 cancers among women																		
Breast	1	123.1	0.1	124.2	0.0	0.8 ^g	1	88.3	1.1 ^g	91.9	-0.3	1	91.9	-0.1				
Lung and bronchus	2	54.1	-0.9 ^g	55.7	-0.9 ^g	-1.0 ^g	3	28.3	-0.1	52.7	-0.5	3	26.0	-1.3 ^g				
Colon and rectum	3	36.6	-3.2 ^g	35.7	-3.2 ^g	-3.6 ^g	2	29.2	-2.6 ^g	40.1	-2.3 ^g	2	30.6	-2.8 ^g				
Corpus and uterus, NOS	4	25.3	1.1 ^g	25.8	1.0 ^g	2.4 ^g	5	17.7	2.3 ^g	22.9	1.5	4	21.1	1.6 ^g				
Thyroid	5	20.3	5.6 ^g	21.3	5.6 ^g	5.9 ^g	4	20.4	5.7 ^g	12.9	5.2 ^g	5	19.3	5.3 ^g				

TABLE 3. Continued

Sex/Cancer Site or Type ^c	All Races and Ethnicities						White ^b		Black ^b		API ^b		AI/AN (CHSDA) ^b		Hispanic ^b		Non-Hispanic ^b					
	2003-2012 AAPC ^e	2008-2012 AAPC ^e	Rank	Rate ^d	2003-2012 AAPC ^e	Rank	Rate ^d	2003-2012 AAPC ^e	Rank	Rate ^d	2003-2012 AAPC ^e	Rank	Rate ^d	2003-2012 AAPC ^e	Rank	Rate ^d	2003-2012 AAPC ^e	Rank				
Non-Hodgkin lymphoma	6	16.0	-1.0 ^a	-1.7 ^a	7	16.5	-1.1 ^a	8	11.8	-0.3	6	10.8	-0.1	6	13.5	-3.0 ^a	6	15.2	-0.7	7	16.1	-1.0 ^a
Melanoma of the skin	7	15.9	1.4 ^a	-0.1	6	18.3	1.5	27	1.0	-1.3	21	1.2	-1.4	16	5.2	0.5	18	4.0	-1.7 ^a	6	17.5	1.8 ^a
Ovary ^f	8	11.9	-2.0 ^a	-2.0 ^a	8	12.3	-2.1 ^a	11	9.4	-1.3 ^a	7	9.0	-0.9 ^a	8	11.8	-0.3	8	10.6	-2.1 ^a	8	12.0	-2.0 ^a
Kidney and renal pelvis	9	11.3	0.9 ^a	-1.1	9	11.4	1.0 ^a	7	12.7	2.2 ^a	13	4.9	0.1	5	18.3	0.6	7	11.8	1.3 ^a	9	11.3	0.9 ^a
Pancreas	10	10.9	0.7 ^a	0.7 ^a	11	10.6	0.7 ^a	5	14.2	0.6	8	8.7	1.3 ^a	9	9.6	-1.6	9	10.3	0.3	10	11.0	0.8 ^a
Leukemia	11	10.3	0.0	0.0	10	10.6	-0.1	12	8.3	0.6	12	6.2	0.5	11	8.9	0.6	11	8.9	-0.1	11	10.3	0.0
Urinary bladder	12	9.0	-1.4 ^a	-1.4 ^a	12	9.5	-1.4 ^a	14	6.6	-0.8 ^a	15	3.8	-1.5	17	4.9	1.6	14	5.1	-2.3 ^a	12	9.4	-1.2 ^a
Cervix uteri	13	7.7	-1.3 ^a	-1.3 ^a	13	7.5	-1.1 ^a	10	9.8	-2.3 ^a	11	6.3	-3.0 ^a	10	9.4	-0.5	10	10.2	-3.9 ^a	13	7.4	1.1 ^a
Oral cavity and pharynx	14	6.3	0.4 ^a	0.4 ^a	14	6.4	0.7 ^a	15	5.1	-1.2 ^a	14	4.9	-0.6	15	5.2	-1.1	17	4.2	0.2	14	6.6	0.5 ^a
Brain and other nervous system	15	5.6	-1.0 ^a	-1.8 ^a	15	6.1	-0.8 ^a	17	3.5	-0.7	16	3.1	-0.9 ^a	18	3.8	1.6	16	4.5	-1.6 ^a	15	5.8	-0.7 ^a
Myeloma	16	5.1	0.3	0.5	16	4.4	0.0	9	10.9	0.9 ^a	17	2.9	0.1	14	5.3	-1.8	15	5.1	-0.6	16	5.1	0.4
Stomach	17	4.6	-0.9 ^a	0.2	17	4.0	-1.0 ^a	13	7.9	-1.2 ^a	9	8.5	-2.8 ^a	13	6.6	-1.4	12	7.8	-2.2 ^a	17	4.3	-1.0 ^a
Liver and intrahepatic bile duct	18	3.9	3.0 ^a	2.3 ^a	18	3.5	3.6 ^a	16	4.8	3.4 ^a	10	7.9	-1.2	12	8.9	2.2	13	7.2	2.4 ^a	18	3.6	2.9 ^a

Abbreviations: AAPC, average annual percent change; AI/AN, American Indian/Alaska Native; API, Asian/Pacific Islander; CHSDA, Indian Health Service Contract Health Services Delivery Area; NOS, not otherwise specified.

^aSource: National Program of Cancer Registries (NPCR) and Surveillance, Epidemiology, and End Results (SEER) areas reported by the North American Association of Central Cancer Registries (NAACCR) as meeting high-quality incidence data standards for the specified time periods (2008-2012 rates for all races/ethnicities, white, black, AI/AN, API, Hispanic, and non-Hispanic [48 states: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, 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]; 2003-2012 AAPCs for all races/ethnicities, white, black, AI/AN, API, Hispanic, and non-Hispanic [45 states: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, 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, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, Wyoming]).

^bWhite, black, API, and AI/AN (CHSDA 2012 counties) include Hispanic and non-Hispanic; the race and ethnicity categories are not mutually exclusive. AI/AN (CHSDA 2012) statistics exclude data from Kansas.

^cCancers are listed in descending rank of sex-specific, age-adjusted rates for 2008 through 2012 for all racial and ethnic groups combined. More than 15 cancers may appear under men and women to include the top 15 cancers in each racial and ethnic group.

^dRates are per 100,000 persons and were age-adjusted to the 2000 US standard population (19 age groups: ages <1 year, 1-4 years, 5-9 years, ..., 80-84 years, ≥85 years; Census publication p25-1130 [US Bureau of the Census, Current Population Reports, p25-1130. Washington, DC: US Government Printing Office; 2000]).

^eThe AAPC is a weighted average of the annual percent change (APC) calculated by joinpoint analyses with up to 2 joinpoints yielding up to 3 trend segments based on rates per 100,000 persons and age adjusted to the 2000 US standard population (19 age groups; Census publication p25-1130). For the joinpoint analysis, the Joinpoint Regression Program was used (version 4.2.0.0, April 2015; Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD).

^fFor all sites, myelodysplastic syndromes are included for the rate calculations but not for the APC calculations; they are excluded from cancer-specific analyses. Ovary excludes borderline tumors.

^gThe AAPC is statistically significantly different from zero (2-sided Z test; $P < .05$).

TABLE 4. US Cancer Death Rates for 2008 to 2012 and Fixed-Interval Trends From 2003 to 2012 for the Top Cancers by Sex, Race, and Ethnicity^a

Sex/Cancer Site or Type ^c	All Races and Ethnicities																								
	2003-2012			2008-2012			White ^b			Black ^b			API ^b			AI/AN (CHSDA) ^b			Hispanic ^b			Non-Hispanic ^b			
	Rank	Rate ^d	AAPC ^e	Rank	Rate ^d	AAPC ^e	Rank	Rate ^d	AAPC ^e	Rank	Rate ^d	AAPC ^e	Rank	Rate ^d	AAPC ^e	Rank	Rate ^d	AAPC ^e	Rank	Rate ^d	AAPC ^e	Rank	Rate ^d	AAPC ^e	
All sites	171.2	-1.5 ^f	-1.5 ^f	1	170.9	-1.4 ^f	1	170.9	-1.4 ^f	202.0	-2.1 ^f	1	106.6	-1.1 ^f	156.1	-1.1 ^f	119.3	-1.2 ^f	175.4	-1.4 ^f	175.4	-1.4 ^f	175.4	-1.4 ^f	
Both sexes	207.9	-1.7 ^f	-1.7 ^f	2	206.4	-1.6 ^f	2	206.4	-1.6 ^f	261.5	-2.6 ^f	2	128.4	-1.5 ^f	186.7	-1.1	148.0	-1.5 ^f	212.4	-1.7 ^f	212.4	-1.7 ^f	212.4	-1.7 ^f	
Men	145.4	-1.4 ^f	-1.4 ^f	3	145.6	-1.3 ^f	3	145.6	-1.3 ^f	166.3	-1.6 ^f	3	91.2	-0.8 ^f	133.9	-1.3 ^f	99.4	-1.0 ^f	149.3	-1.4 ^f	149.3	-1.4 ^f	149.3	-1.4 ^f	
Women	2.2	-1.8 ^f	-1.8 ^f	15	2.2	-1.8 ^f	15	2.2	-1.8 ^f	2.1	-2.0 ^f	15	1.9	-0.6	1.7	-0.9	2.2	-2.2 ^f	2.2	-1.7 ^f	2.2	-1.7 ^f	2.2	-1.7 ^f	
Children (ages 0-14 years)	2.4	-1.5 ^f	-0.2	16	2.4	-1.6 ^f	16	2.4	-1.6 ^f	2.3	-2.0 ^f	16	2.1	0.6	1.8	-0.6	2.5	-1.8 ^f	2.3	-2.0 ^f	2.3	-2.0 ^f	2.3	-2.0 ^f	
Children (ages 0-19 years)	59.8	-2.7 ^f	-2.9 ^f	1	59.7	-2.6 ^f	1	59.7	-2.6 ^f	73.1	-3.4 ^f	1	34.0	-2.0 ^f	49.1	-0.9	29.5	-3.1 ^f	62.2	-2.6 ^f	62.2	-2.6 ^f	62.2	-2.6 ^f	
Top 17 cancers among men ^c	21.4	-3.4 ^f	-3.4 ^f	2	19.8	-3.3 ^f	2	19.8	-3.3 ^f	46.3	-3.9 ^f	4	9.4	-3.5 ^f	20.2	-2.8 ^f	17.8	-3.0 ^f	21.6	-3.4 ^f	21.6	-3.4 ^f	21.6	-3.4 ^f	
Lung and bronchus	18.6	-2.8 ^f	-2.8 ^f	3	18.0	-3.0 ^f	3	18.0	-3.0 ^f	26.9	-2.6 ^f	3	13.0	-1.1 ^f	18.8	-2.5	15.6	-1.5 ^f	18.8	-2.8 ^f	18.8	-2.8 ^f	18.8	-2.8 ^f	
Prostate	12.6	0.3 ^f	0.3 ^f	4	12.5	0.5 ^f	4	12.5	0.5 ^f	15.0	-0.5	5	8.4	0.0	9.3	-1.6	9.8	0.2	12.8	0.4 ^f	12.8	0.4 ^f	12.8	0.4 ^f	
Colon and rectum	9.4	-0.9 ^f	-0.9 ^f	5	9.7	-0.8 ^f	5	9.7	-0.8 ^f	7.9	-1.6 ^f	7	5.1	0.7	6.7	1.6	6.1	-0.7	9.5	-0.8 ^f	9.5	-0.8 ^f	9.5	-0.8 ^f	
Pancreas	8.8	2.8 ^f	2.8 ^f	7	8.1	3.0 ^f	7	8.1	3.0 ^f	12.5	2.7 ^f	2	14.5	-0.9 ^f	4	13.9	4.2 ^f	12.9	1.7 ^f	8.5	2.8 ^f	8.5	2.8 ^f	8.5	2.8 ^f
Leukemia	7.9	-2.1 ^f	-2.1 ^f	6	8.2	-2.1 ^f	6	8.2	-2.1 ^f	5.7	-1.0	8	5.0	-2.2 ^f	9	5.7	0.5	6.3	-1.1 ^f	8.0	-2.2 ^f	8.0	-2.2 ^f	8.0	-2.2 ^f
Liver and intra-hepatic bile duct	7.7	0.0	0.0	8	7.7	0.0	8	7.7	0.0	5.3	-0.7	9	3.0	1.1	4.2	3.4	3.9	-1.2	7.9	0.1	7.9	0.1	7.9	0.1	
Non-Hodgkin lymphoma	7.5	-0.8 ^f	-0.8 ^f	9	7.7	0.0	9	7.7	0.0	7.0	-4.5 ^f	12	2.8	-2.4	5.6	-4.9 ^f	4.3	0.1	7.7	-0.7 ^f	7.7	-0.7 ^f	7.7	-0.7 ^f	
Urinary bladder	5.7	-0.7 ^f	-0.7 ^f	10	5.9	-0.7 ^f	10	5.9	-0.7 ^f	5.6	-1.3 ^f	11	2.9	1.5	8.7	-0.9	5.0	-1.4	5.8	-0.7 ^f	5.8	-0.7 ^f	5.8	-0.7 ^f	
Esophagus	5.3	0.1	0.1	11	5.7	0.2	11	5.7	0.2	3.1	0.0	13	2.4	0.2	3.2	1.6	3.4	0.3	5.5	0.2	5.5	0.2	5.5	0.2	
Kidney and renal pelvis	4.6	-3.1 ^f	-3.1 ^f	14	4.0	-3.2 ^f	14	4.0	-3.2 ^f	9.2	-3.3 ^f	6	7.9	-4.3 ^f	7	7.4	-3.2	7.2	-3.1 ^f	4.3	-3.3 ^f	4.3	-3.3 ^f	4.3	-3.3 ^f
Brain and other nervous system	4.2	-0.9 ^f	-0.9 ^f	13	4.0	-0.9 ^f	13	4.0	-0.9 ^f	7.6	-1.4 ^f	14	2.2	1.6	3.2	-6.8 ^f	3.5	0.2	4.3	-0.9 ^f	4.3	-0.9 ^f	4.3	-0.9 ^f	
Stomach	4.1	0.1	0.1	12	4.6	0.3	12	4.6	0.3	0.5	-1.6	20	0.4	-0.9	1.5	-0.9	1.0	0.5	4.3	0.3	4.3	0.3	4.3	0.3	
Myeloma	3.8	-0.4	1.1	15	3.7	0.0	15	3.7	0.0	5.0	-3.4 ^f	10	2.9	-1.5	3.6	0.5	2.4	-1.4 ^f	3.9	-0.2	3.9	-0.2	3.9	-0.2	
Melanoma of the skin	1.9	-2.8 ^f	-2.8 ^f	16	1.8	-2.5 ^f	16	1.8	-2.5 ^f	3.6	-4.2 ^f	16	0.8	0.6	1.7	-0.9	1.7	-2.9 ^f	2.0	-2.7 ^f	2.0	-2.7 ^f	2.0	-2.7 ^f	
Oral cavity and pharynx	1.5	1.0 ^f	1.0 ^f	18	1.6	1.1 ^f	18	1.6	1.1 ^f	1.5	0.1	15	1.0	2.2	1.5	-0.9	1.2	3.2 ^f	1.6	1.0 ^f	1.6	1.0 ^f	1.6	1.0 ^f	
Larynx																									
Soft tissue including heart																									

TABLE 4. Continued

Sex/Cancer Site or Type ^c	All Races and Ethnicities				White ^b			Black ^b			AI/AN (CHSDA) ^b			Hispanic ^b			Non-Hispanic ^b		
	Rank	Rate ^d	2008-2012 AAPC ^e	2008-2012 AAPC ^e	Rank	Rate ^d	2003-2012 AAPC ^e	Rank	Rate ^d	2003-2012 AAPC ^e	Rank	Rate ^d	2003-2012 AAPC ^e	Rank	Rate ^d	2003-2012 AAPC ^e	Rank	Rate ^d	2003-2012 AAPC ^e
Top 17 cancers among women ^f	1	37.8	-1.4 ^f	-1.9 ^f	1	39.1	-1.3 ^f	1	35.8	-1.8 ^f	1	32.1	-1.3 ^f	2	13.7	-1.4 ^f	1	39.8	-1.2 ^f
Lung and bronchus	2	21.9	-1.9 ^f	-1.5	2	21.3	-1.9 ^f	2	30.2	-1.4 ^f	2	11.4	-1.4 ^f	1	14.5	-1.3 ^f	2	22.5	-1.8 ^f
Breast	3	13.1	-2.8 ^f	-2.8 ^f	3	12.7	-2.8 ^f	3	17.8	-3.4 ^f	3	9.4	-1.3 ^f	3	9.6	-2.2 ^f	3	13.3	-2.8 ^f
Colon and rectum	4	9.6	0.3 ^f	0.3 ^f	4	9.4	0.4 ^f	4	12.3	-0.2	4	7.3	1.0 ^f	4	7.7	0.0	4	9.8	0.4 ^f
Pancreas	5	7.7	-2.1 ^f	-2.1 ^f	5	8.0	-2.1 ^f	6	6.7	-1.6 ^f	7	4.6	-1.3 ^f	5	5.6	-1.4 ^f	5	7.9	-2.1 ^f
Ovary	6	5.2	-1.0 ^f	-1.0 ^f	6	5.4	-0.9 ^f	8	4.7	-1.3 ^f	9	3.2	1.5 ^f	12	3.2	-5.1	9	4.0	-1.0 ^f
Leukemia	7	4.8	-2.8 ^f	-2.8 ^f	7	5.0	-2.8 ^f	12	3.5	-2.3 ^f	8	3.4	-1.9 ^f	8	3.6	-5.5 ^f	7	4.3	-1.2 ^f
Non-Hodgkin lymphoma	8	4.4	1.1 ^f	1.1 ^f	8	4.1	0.9 ^f	5	7.7	1.6 ^f	10	2.8	3.1 ^f	10	3.5	-0.9	10	3.5	2.3 ^f
Corpus and uterus, NOS	9	3.5	2.0 ^f	3.4 ^f	10	3.3	2.2 ^f	10	4.3	1.6 ^f	5	6.1	-1.4	6	6.3	-1.2	6	5.6	1.1 ^f
Liver and intrahepatic bile duct	10	3.5	-0.2	-0.2	9	3.8	-0.2	15	2.1	0.4	12	1.6	0.2	14	1.9	-0.9	12	2.4	0.1
Brain and other nervous system	11	2.7	-1.2 ^f	0.8	12	2.4	-1.2 ^f	7	5.3	-1.5 ^f	13	1.4	0.2	13	2.3	-6.6	14	2.3	-1.3
Myeloma	12	2.5	-1.4 ^f	-1.4 ^f	11	2.6	-1.4 ^f	13	2.5	-1.1	14	1.2	-0.1	7	4.7	1.9	13	2.4	-0.8
Kidney and renal pelvis	13	2.4	-2.6 ^f	-2.6 ^f	15	2.1	-2.7 ^f	9	4.4	-2.8 ^f	6	4.7	-3.3 ^f	9	3.6	-3.5 ^f	8	4.2	-2.7 ^f
Stomach	14	2.3	-0.9 ^f	-0.9 ^f	14	2.1	-0.6 ^f	11	4.0	-2.2 ^f	11	1.8	-3.1 ^f	11	3.5	-1.4	11	2.7	-2.3 ^f
Cervix uteri	15	2.2	-0.5 ^f	-0.5 ^f	13	2.2	-0.3	14	2.5	-1.5 ^f	16	0.9	-1.5	18	1.1	-0.9	15	1.3	-1.3
Urinary bladder	18	1.4	-1.2 ^f	-1.2 ^f	18	1.3	-1.1 ^f	18	1.3	-2.3 ^f	15	1.2	-1.2	17	1.2	-0.9	19	0.8	0.2
Oral cavity and pharynx	20	0.7	-1.2 ^f	-1.2 ^f	20	0.7	-1.5 ^f	19	1.0	0.8	20	0.8	-2.2	15	1.8	-4.4	16	1.3	0.2
Gallbladder																			

Abbreviations: AAPC, average annual percent change; AI/AN, American Indian/Alaska Native; API, Asian/Pacific Islander; CHSDA, Indian Health Service Contract Health Services Delivery Area; NOS, not otherwise specified.

^aSource: National Center for Health Statistics public-use data file for the total United States, 1975-2012.

^bWhite, black, API, and AI/AN (CHSDA 2012 counties) populations include Hispanic and non-Hispanic; the race and ethnicity categories are not mutually exclusive.

^cCancers are listed in descending rank order of sex-specific, age-adjusted incidence rates for 2008 through 2012 for all racial and ethnic groups combined. More than 15 cancers may appear under men and women to include the top 15 cancers in each racial and ethnic group.

^dRates are per 100,000 persons and were age-adjusted to the 2000 US standard population (19 age groups; ages <1 year, 1-4 years, 5-9 years, . . . , 80-84 years, ≥85 years; Census publication p25-1130 [US Bureau of the Census, Current Population Reports, p25-1130, Washington, DC: US Government Printing Office; 2000]).

^eThe AAPC is a weighted average of the annual percent change and is calculated by joinpoint analyses with up to 2 joinpoints yielding up to 3 trend segments based on rates per 100,000 persons and age adjusted to the 2000 US standard population (19 age groups; Census publication p25-1130). For joinpoint analysis, the Joinpoint Regression Program was used (version 4.2.0.0, April 2015; Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD).

^fThe AAPC is statistically significantly different from zero (2-sided Z test; $P < .05$).

^gThe statistic could not be calculated. The AAPC is based on <10 cases for at least 1 year within the time interval.

TABLE 5. Average Annual Number of Liver and Intrahepatic Bile Duct Cancer Cases (N = 24,777), Incidence Rates and Average Annual Percentage Change in Incidence Rate From 2008 to 2012 by Sex, Race or Ethnicity, and Age Group for Areas in the United States With High-Quality Incidence Data^a

Characteristic	Both Sexes			Men		Women			
	Average Annual No. of Cases	Rate ^b	2008-2012 AAPC ^c	Average Annual No. of Cases	Rate ^b	2008-2012 AAPC ^c	Average Annual No. of Cases	Rate ^b	2008-2012 AAPC ^c
Overall ^d	24,777	7.4	2.3 ^e	17,835	11.4	2.2 ^e	6,941	3.9	2.2 ^e
Race or ethnicity									
NH white	15,417	6.0	2.8 ^e	11,102	9.3	2.8 ^e	4,315	3.2	3.5 ^e
NH black	3,604	9.9	3.9 ^e	2,671	16.5	3.9 ^e	932	4.8	3.4 ^e
NH AI/AN (CHSDA)	184	14.9	3.4 ^e	119	21.0	4.0 ^e	64	9.9	2.7
NH API	1,891	13.8	-1.2 ^e	1,315	20.9	-1.2 ^e	576	8.0	-1.1
Hispanic ^d	3,682	12.7	0.7	2,627	19.3	-0.1	1,054	7.2	2.4 ^e
Age group, y									
<40	551	0.4	0.2	336	0.4	-0.5	215	0.3	1.3
40-44	358	1.8	-1.5 ^e	253	2.5	-2.6 ^e	105	1.0	1.5
45-49	1,109	5.1	-2.5 ^e	862	8.1	-3.3 ^e	247	2.3	0.7
50-54	2,897	13.6	-2.5	2,345	22.4	-3.5	552	5.1	1.3
55-59	4,588	24.1	3.9 ^e	3,726	40.5	3.2 ^e	862	8.8	6.5 ^e
60-64	3,997	24.7	8.9 ^e	3,129	40.4	9.7 ^e	867	10.3	5.9 ^e
65-69	3,034	25.0	3.8 ^e	2,176	38.1	3.8 ^e	858	13.4	3.5 ^e
70-74	2,597	28.7	2.5 ^e	1,742	42.2	2.5 ^e	855	17.4	2.1 ^e
75-79	2,311	32.6	2.1 ^e	1,449	47.0	-0.4	861	21.5	2.4 ^e
80-84	1,845	33.2	2.7 ^e	1,084	48.8	2.4 ^e	761	22.8	2.5 ^e
≥85	1,491	27.9	1.8 ^e	733	41.9	1.8 ^e	758	21.1	1.4 ^e

Abbreviations: AI/AN, American Indian/Alaska Native; AAPC, average annual percent change; API, Asian/Pacific Islander; CHSDA, Contract Health Services Delivery Area; NH, non-Hispanic.
^aSource: National Program of Cancer Registries and Surveillance, Epidemiology, and End Results areas reported by North American Association of Central Cancer Registries as meeting high-quality incidence data standards for the specified time. Rates are listed from 2008 to 2012 for NH whites, NH blacks, NH AI/AN (CHSDA 2012 counties), NH API, and Hispanics (48 states: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, 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).
^bRates are per 100,000 persons and were age-adjusted to the 2000 US standard population (19 age groups; ages <1 year, 1-4 years, 5-9 years, ..., 80-84 years, ≥85 years; Census publication p25-1130 [US Bureau of the Census, Current Population Reports, p25-1130. Washington, DC: US Government Printing Office; 2000]).
^cThe AAPC is a weighted average of the APCs calculated by joinpoint analysis with up to 2 joinpoints, yielding up to 3 trend segments based on rates per 100,000 persons and age-adjusted to the 2000 US standard population (19 age groups; Census publication p25-1130). For joinpoint analysis, the Joinpoint Regression Program was used (version 4.2.0.0, April 2015; Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD).
^dThis table excludes unknown Hispanic and Hispanic other/unknown race.
^eThe AAPC is statistically significantly different from zero (2-sided Z test; P < .05).

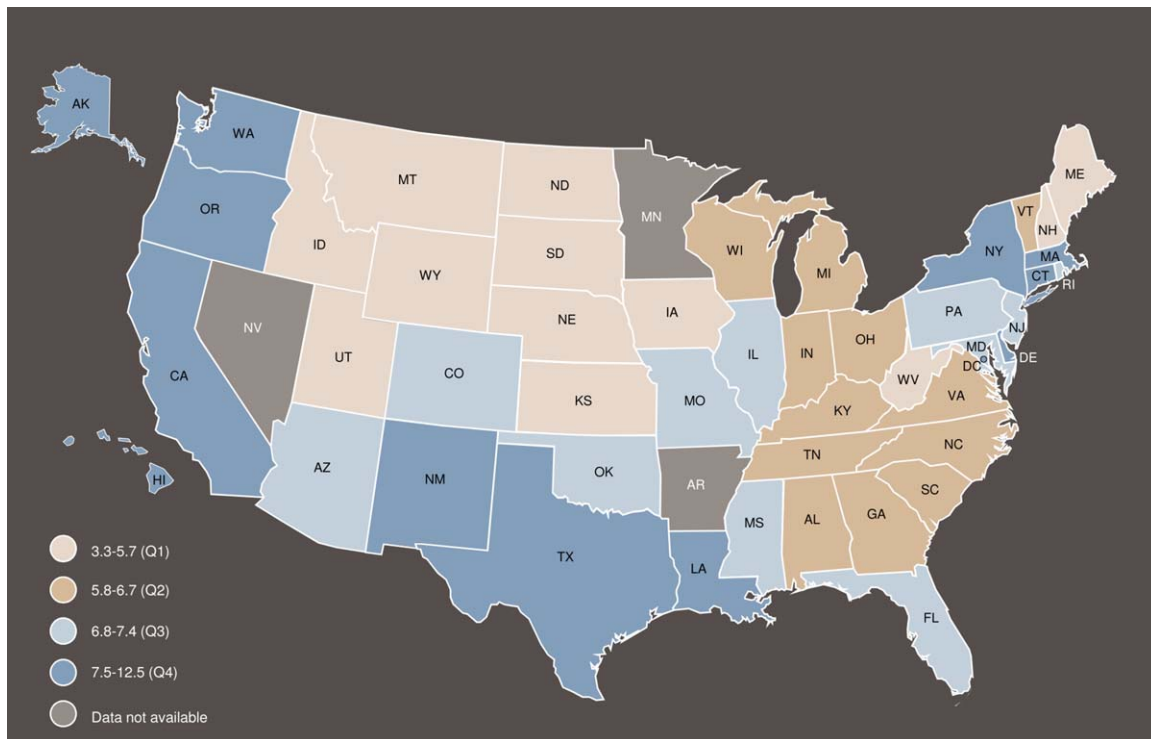


Figure 1. Age-adjusted incidence rates for 2008 to 2012 of liver and intrahepatic bile duct cancer are illustrated by state for areas in the United States with high-quality incidence data. Rates are per 100,000 persons and were age-adjusted to the 2000 US standard population (19 age groups: ages <1 year, 1-4 years, 5-9 years, . . . , 80-84 years, ≥85 years [Census publication p25-1130; US Bureau of the Census, Current Population Reports, p25-1130. Washington, DC: US Government Printing Office; 2000]). Source: National Program of Cancer Registries and Surveillance, Epidemiology, and End Results areas reported by the North American Association of Central Cancer Registries as meeting high-quality incidence data standards for the specified time. Rates from 2008 to 2012 for non-Hispanic (NH) whites, NH blacks, NH American Indians/Alaska Natives (Contract Health Services Delivery Area 2012 counties), NH Asians/Pacific Islanders, and Hispanics (48 states: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, 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).

year), but they increased or remained stable among other racial and ethnic groups.

Among women, the overall cancer incidence rates declined slightly from 2003 to 2012 for women in all racial and ethnic groups combined, but this decline was not statistically significant for most racial and ethnic groups. Whereas breast cancer incidence rates remained stable during this period for women overall, rates increased among black women (0.8% per year) and API women (1.1% per year). During 2003 through 2012, lung cancer incidence rates decreased among women of all racial and ethnic groups, except API and AI/AN. Colorectal cancer incidence rates decreased among women of all racial and ethnic groups; thyroid cancer incidence rates increased among women of all groups; and uterus cancer incidence rates increased among women of all groups, except AI/AN. Like in men, trends in incidence rates dur-

ing the past decade for most cancers in each racial and ethnic group were similar in direction to those for all women combined, but some trends were not statistically significant. Oral cancer incidence rates decreased among black women but increased or remained stable among most racial and ethnic groups, and melanoma incidence rates increased among white women but decreased among Hispanic women.

Current Cancer Death Rates and Trends by Race and Ethnicity

Five-year (2008-2012) death rates and fixed-interval mortality trends from 2003 to 2012 were analyzed by sex and by race and ethnicity (Table 4). For all cancer sites combined, cancer death rates (per 100,000) for 2008 to 2012 were higher among men than among women (207.9 vs 145.4). During 2008 through 2012, black men and

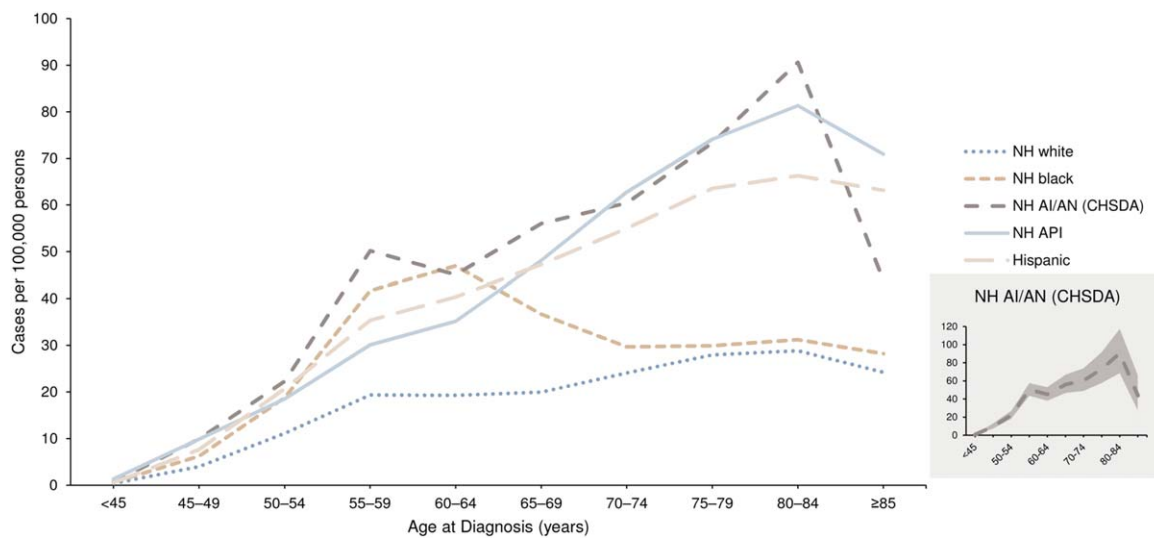


Figure 2. Age-specific incidence rates from 2008 to 2012 of liver and intrahepatic bile duct cancer are illustrated by race or ethnicity for areas in the United States with high-quality incidence data. Rates are per 100,000 persons and were age-adjusted to the 2000 US standard population (19 age groups: ages <1 year, 14 years, 5-9 years, . . . , 80-84 years, ≥85 years [Census publication p25-1130; US Bureau of the Census, Current Population Reports, p25-1130. Washington, DC: US Government Printing Office; 2000]). Source: National Program of Cancer Registries and Surveillance, Epidemiology, and End Results areas reported by the North American Association of Central Cancer Registries as meeting high-quality incidence data standards for the specified time. Rates from 2008 to 2012 for non-Hispanic (NH) whites, NH blacks, NH American Indians/Alaska Natives (AI/AN) (Contract Services Delivery Area [CHSDA] 2012 counties), NH Asians/Pacific Islanders (API), and Hispanics (48 states: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, 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).

women had the highest cancer death rates compared with all other racial and ethnic groups. Lung cancer was the leading cause of cancer death among both men and women of all racial and ethnic groups, except among Hispanic women, for whom mortality from breast cancer was higher. Among men, lung cancer was followed by prostate cancer and then colorectal cancer as the leading causes of cancer death, except among API men, for whom liver cancer replaced prostate cancer as the second leading cause of cancer death. Among women of all racial and ethnic groups, except Hispanic women, lung cancer was followed by breast and colorectal cancers as the leading causes of cancer death; among Hispanic women, breast cancer mortality was followed by lung cancer and colorectal cancer mortality.

From 2003 to 2012, death rates declined for the most common cancers (lung, prostate, colorectal, breast) among men and women of all racial and ethnic groups except for statistically insignificant decreases in lung cancer and colorectal cancer among AI/AN men and in colorectal cancer among AI/AN women. Death rates for most cancer sites declined or were stable from 2003 to 2012 among men and women of each racial and ethnic group, except for liver can-

cer, which increased for most racial and ethnic groups except for API men and women and AI/AN women; pancreatic cancer, which increased among white men and women and API women; soft tissue cancer, which increased among white and Hispanic men; uterine cancer, which increased among white, black, API, and Hispanic women; and leukemia, which increased among API women.

Incidence of Liver Cancer

Rates of incident liver and intrahepatic bile duct (liver) cancer were examined by mutually exclusive racial or ethnic groups, gender, and age during 2008 through 2012 to better describe demographic patterns (Table 5). Among men and women, liver cancer incidence rates were highest among NH AI/ANs, followed by NH APIs, and Hispanics. Among all racial or ethnic groups, liver cancer incidence rates among men were more than twice those among women. Among men, liver cancer incidence rates increased during 2008 through 2012 among NH white, NH black, and NH AI/AN men, but decreased among NH API men, and were stable among Hispanic men. A different pattern emerged for liver cancer incidence rates among women, which increased among Hispanic women

and among NH white and NH black women. Among both men and women, liver cancer incidence rates increased significantly from 2008 to 2012, beginning at age 55 years, and the largest AAPC was observed among the group ages 60 to 64 years among men and the group ages 55 to 59 years among women. Liver cancer incidence rates among both men and women increased with age for almost all groups until age ≥ 85 years. State-specific liver cancer incidence rates ranged 3-fold, from 3.3 to 12.5 per 100,000 persons (Fig. 1). Liver cancer incidence rates were highest in Pacific states, in states on the southern US border, in the District of Columbia, and in a few states in the Northeast, including Delaware, Connecticut, Massachusetts, and New York.

The age distribution of liver cancer diagnosed during 2008 through 2012 varied across racial or ethnic groups (Fig. 2). Although liver cancer incidence rates generally increased with age, the rate of increase varied by racial or ethnic group. Furthermore, liver cancer incidence rates during 2008 through 2012 among NH blacks peaked at an earlier age (60-64 years), and then decreased at older ages. The NH AI/AN population also had an increase at younger ages (ages 55-59 years); however, liver cancer incidence rates continued to increase among this group up to ages 80 to 84 years. The statistical uncertainty in the liver cancer incidence rates by age group among the NH AI/AN population was mostly caused by the smaller number of cases at each age, as indicated in the Figure 2 inset. Because of this statistical instability, the incidence rates for NH AI/AN populations are not provided separately in later analyses. NH API populations experienced the highest liver cancer incidence rates for those aged < 50 years and ≥ 65 years (after NH AI/AN populations), but Hispanic and NH blacks had higher rates in the group ages 50 to 64 years. The lowest liver cancer incidence rates for each age group were observed among NH white populations.

Figure 3 illustrates the cohort rate ratios and 95% CIs by race or ethnicity for liver cancer incidence relative to the experience of the 1943 reference birth cohort. Among NH white, NH black, and Hispanic men and women, the cohort rate ratio was < 1.0 for the 1913 to 1938 birth cohorts. The rate ratio then sharply increased for birth cohorts 1948 through 1953. The rate ratio for birth cohorts 1953 through 1968 slightly decreased among NH whites and Hispanics but decreased sharply among NH blacks. In contrast, the cohort relative risk remained unchanged for NH APIs, signifying a minimal birth-cohort effect.

Figure 4 illustrates liver cancer incidence rates by age for cases diagnosed during 3 time intervals: 1992 to 1996, 2000 to 2004, and 2008 to 2012. Liver cancer incidence rates in general, as noted above, continued to increase with advancing age for each diagnosis period. However, during 2008 through 2012, liver cancer incidence rates among NH blacks were highest among persons ages 55 to 59 years, who are in the 1953 birth cohort (born during 1948-1957). A similar pattern is observed among NH whites and Hispanics, for whom there was a sharp increase among those ages 55 to 59 years during 2008 through 2012, although liver cancer incidence rates continued to increase with age. Among NH whites, NH blacks, and Hispanics, liver cancer incidence rates were generally highest for the most recent (2008-2012) diagnosis years and lowest for the 1992 to 1996 diagnosis years. Among Hispanics, there was a large difference between diagnosis years for every age; whereas, among NH whites and NH blacks, the largest difference was for those ages 50 to 69 years. The differences by diagnosis year were less pronounced among NH APIs than among other subgroups.

Table 6 presents incidence-based mortality data for liver cancer in the SEER-18 areas during 2008 through 2012. More than half of these deaths (53%) occurred among NH whites. The median age at death from liver cancer was younger among NH blacks (median age, 61 years) and Hispanics (median age, 64 years) than among NH whites (median age, 66 years) and NH APIs (median age, 68 years). The median age at death was 9 years older among women (median age, 72 years) than among men (median age, 63 years), but this difference ranged from 4 years among NH blacks to 10 years among NH APIs. More than 379,000 person-years of life were lost to liver cancer during 2008 through 2012. The average person-years of life that were lost to liver cancer death was higher among NH blacks (average, 22 PYLL) and Hispanics (average, 20 PYLL) than among NH APIs and NH whites (average, 18 PYLL for both). Although 74% of total PYLL were among men, the APYLL was similar among men (19 APYLL) and women (17 APYLL).

HCV and liver cancer-associated mortality from 1999 to 2013 is illustrated in Figure 5. Among persons for whom both HCV and liver cancer were listed as causes of death, those born during 1945 through 1965 had the largest increase in mortality from 1999 to 2013 relative to the other birth-year categories (Fig. 5A). Considering the differences in age between birth cohorts, those born during 1945 through 1965 had substantially higher rates of HCV and liver cancer-associated deaths

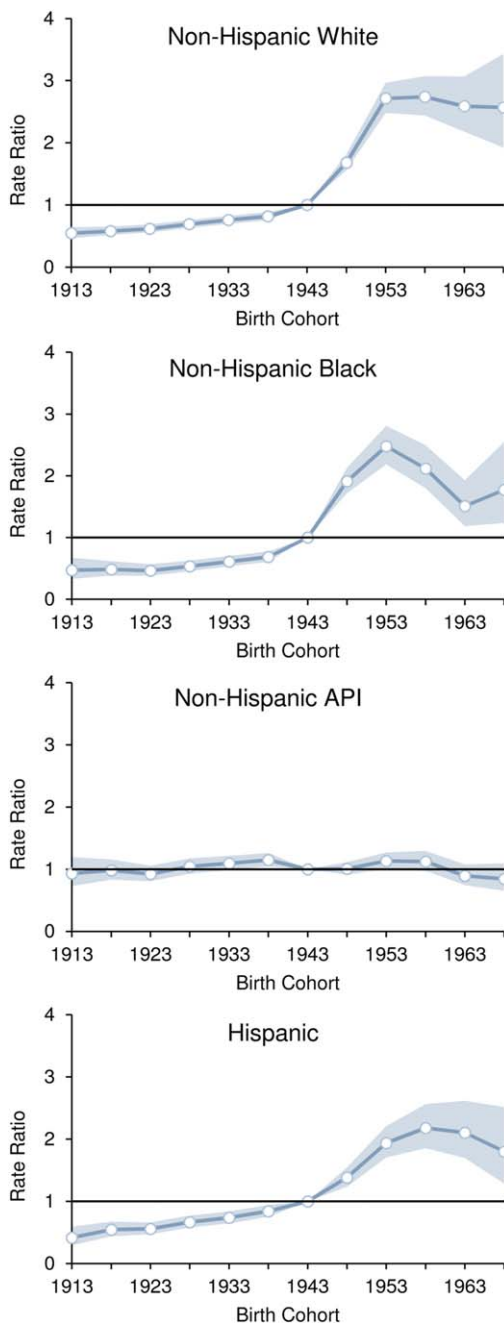


Figure 3. Cohort rate ratios (horizontal blue lines) and 95% confidence intervals (blue shading) are illustrated for the incidence of liver and intrahepatic bile duct cancer by race or ethnicity relative to the experience of the 1943 reference birth cohort (Surveillance, Epidemiology, and End Results [SEER]-13 areas, 1992-2012). The vertical lines indicate a rate ratio of 1 (no difference between a select birth cohort and the reference cohort). API indicates Asian/Pacific Islander. Source: SEER-13 areas covering about 14% of the US population (Connecticut, Hawaii, Iowa, Utah, and New Mexico); the Alaska Native Tumor Registry; rural Georgia; and the metropolitan areas of San Francisco, Los Angeles, San Jose-Monterey, Detroit, Atlanta, and Seattle-Puget Sound).

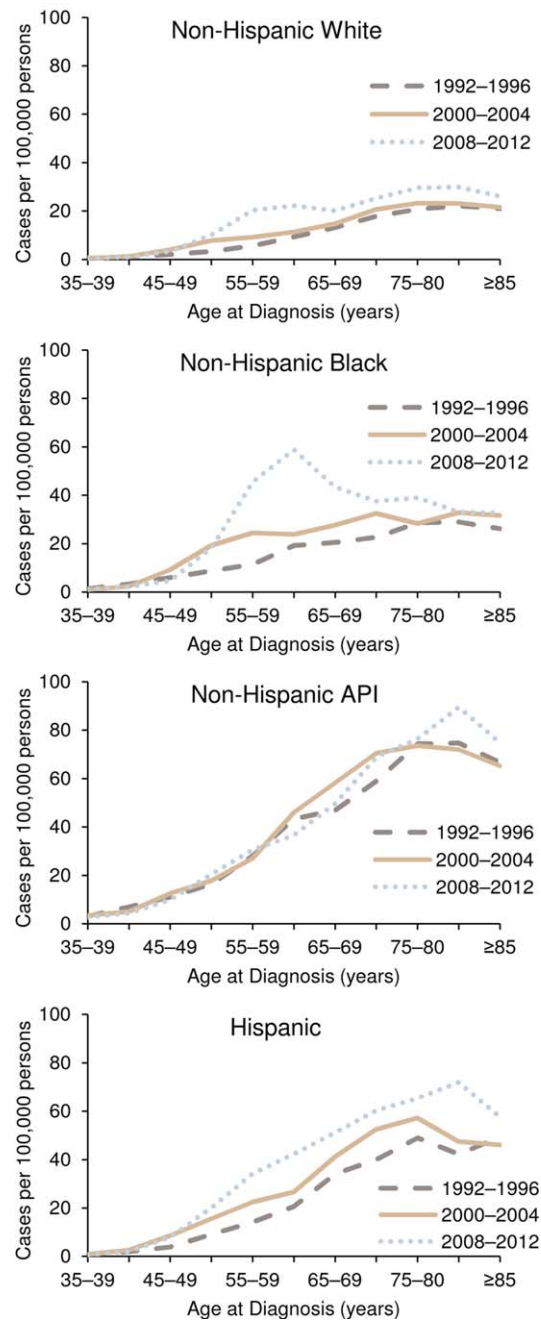


Figure 4. Age-specific liver and intrahepatic bile duct cancer incidence rates are illustrated by race or ethnicity and by age and year of diagnosis in the Surveillance, Epidemiology, and End Results (SEER)-13 areas from 1992 to 2012. Rates are per 100,000 persons. API indicates Asian/Pacific Islander. Source: SEER-13 areas covering about 14% of the US population (Connecticut, Hawaii, Iowa, Utah, and New Mexico); the Alaska Native Tumor Registry; rural Georgia; and the metropolitan areas of San Francisco, Los Angeles, San Jose-Monterey, Detroit, Atlanta, and Seattle-Puget Sound).

TABLE 6. Distribution of Deaths, Median Age at Death, and Person-Years of Life Lost From Liver and Intrahepatic Bile Duct Cancer, by Sex, and Race or Ethnicity, Surveillance, Epidemiology, and End Results-18 Areas, 2008 to 2012^a

Sex, Race, and Ethnicity ^b	Deaths by Race, % ^c	Deaths by Sex, % ^c	Median Age at Death, y	Total No. of PYLL ^d	PYLL by Race, % ^d	PYLL by Sex, % ^d	Average PYLL per Death ^d
Total	100		65	379,464	100		19
Men		73	63	270,741		74	19
Women		27	72	93,294		26	17
Non-Hispanic, white	53		66	192,278	51		18
Men		73	64	137,046		74	18
Women		27	73	47,180		26	17
Non-Hispanic, black	13		61	55,030	15		22
Men		76	60	40,038		76	21
Women		24	64	12,733		24	21
Non-Hispanic, API	15		68	56,248	15		18
Men		69	65	39,543		73	19
Women		31	75	14,570		27	16
Hispanic	18		64	70,588	19		20
Men		73	62	50,486		74	20
Women		27	71	17,308		26	18

Abbreviations: API, Asian/Pacific Islander; PYLL, person-years of life lost.

^aSource: Surveillance, Epidemiology, and End Results (SEER)-18 areas covering about 28% of the US population (10 state registries [Connecticut, Georgia, Greater California, Hawaii, Iowa, Kentucky, Louisiana, New Jersey, New Mexico, and Utah], 3 Native American registries [the Alaska Native Tumor Registry, Arizona Indians, and the Cherokee Nation Cancer Registry], and 5 metropolitan area registries [metropolitan Atlanta and rural Georgia, San Francisco-Oakland and San Jose-Monterey, Los Angeles, Detroit, and Seattle-Puget Sound]).

^bThe table excludes individuals of unknown Hispanic and Hispanic other/unknown race.

^cValues indicate incidence-based mortality.

^dPYLL and average PYLL estimates are 5-year totals estimated by using overall, male, and female all-races life tables.

than the preceding or subsequent birth cohorts, particularly for the mid-generational group (Fig. 5B).

DISCUSSION

Ongoing reductions in both the incidence and mortality of cancer overall, and specifically deaths from the most common cancers (female breast, prostate, lung, and colorectal cancers) in most racial and ethnic groups, represent continued progress in specific areas of public health and oncology care.²⁻¹⁷ For example, successful and comprehensive public health tobacco-control strategies remain an important contributing factor to the observed declines in lung cancer incidence and mortality among both men and women.^{11,54-56} To aid in the earlier diagnosis of lung cancer among those who remain at an increased risk from tobacco use, in 2013, the USPSTF recommended routine screening with low-dose computed tomography of persons at high-risk because of their age and cigarette smoking history.⁵⁷ Continuing public health surveillance is needed to monitor the success of these efforts to increase screening in appropriate populations; and resulting reductions in mortality may reflect a decrease in lung cancer mortality rates.

Colorectal cancer incidence and death rates also continue to decline. There is strong evidence to support the finding that screening for colorectal cancer reduces both

the incidence and the mortality of the disease,⁵⁸ and increases in colorectal cancer survival rates during the past 2 decades have been attributed largely to screening.⁵⁹⁻⁶¹ Still, a recent report about the use of colorectal cancer screening indicated that 35% of US adults were not up to date with one of the colorectal cancer screening tests recommended by the USPSTF.⁶² To help increase colorectal cancer screening compliance, the CDC funds the Colorectal Cancer Control Program to implement evidence-based interventions and provide screening and follow-up services for a limited number of eligible individuals.⁶³ In addition, in 2014, the National Colorectal Cancer Roundtable, a coalition aimed at reducing colorectal cancer incidence and mortality, initiated a nationwide goal of increasing colorectal cancer screening prevalence to 80% by 2018.⁶⁴

Breast cancer, as the most commonly diagnosed and second leading cause of cancer death among women, remains an important public health issue. Advances in treatment and early detection contribute to the ongoing decrease in breast cancer mortality among women overall.⁶⁵ However, not all racial and ethnic groups benefit equally in this favorable trend: black women have a higher breast cancer death rate than white women.¹⁷ Efforts are underway to better understand the factors contributing to these observed differences, including surveillance of breast

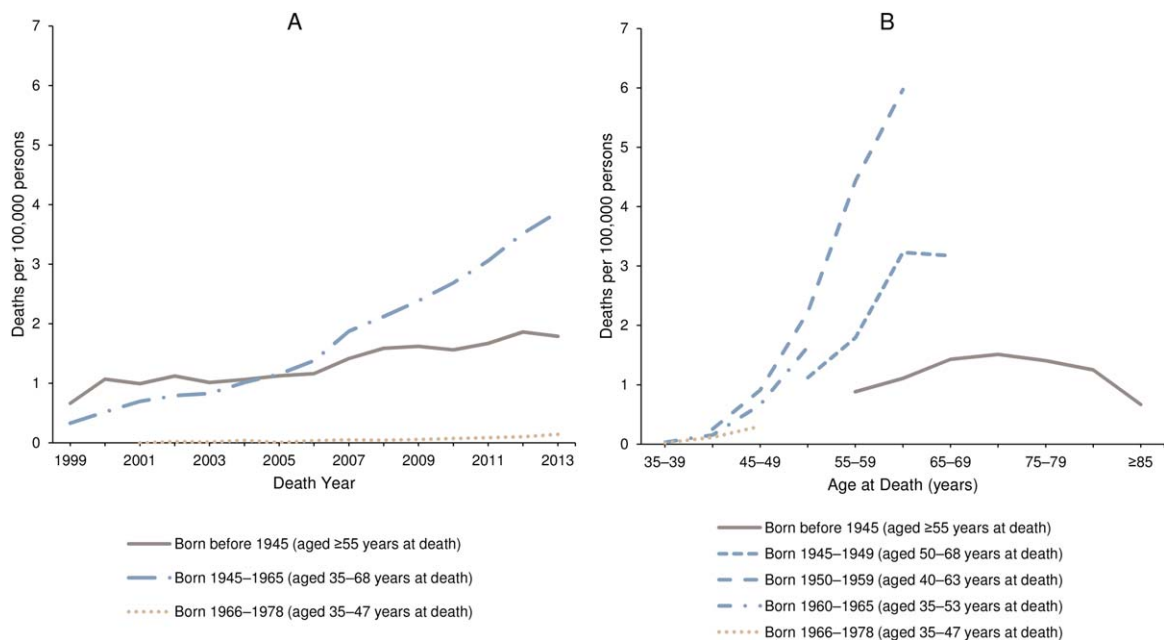


Figure 5. Crude death rates associated with hepatitis C virus and liver or intrahepatic bile duct cancer are illustrated among decedents aged ≥ 35 years according to (A) birth cohort and year and (B) birth cohort and age for the United States from 1999 to 2013. Rates are per 100,000 persons. Hepatitis C virus was defined according to the International Classification of Diseases 10th Revision (ICD-10) codes B17.1 and B18.2. Liver and intrahepatic bile duct cancers were defined by any ICD-10 code in the C22 ICD-10 category. Patients who died from liver or intrahepatic bile duct cancers had hepatitis C and liver or intrahepatic bile duct cancer listed together as any cause of death on their death certificate. Source: National Center for Health Statistics public-use data file for the total United States, 1999 to 2013.

cancer subtypes by different racial and ethnic groups,¹⁷ and to promote the use of evidence-based interventions aimed at groups struggling with access to care, such as CDC's National Breast and Cervical Cancer Early Detection Program.⁶⁶

The continued decrease in prostate cancer incidence likely reflects the continued reduction in the use of prostate-specific antigen testing.⁶⁷⁻⁷⁰ In 2008, the USPSTF concluded that there was insufficient evidence to recommend prostate cancer screening among men aged ≥ 75 years; and, in 2012, it further recommended against screening for all men,⁷¹ likely contributing to the observed reduction in incidence rates since that time.^{15-17,72} Close public health surveillance of both prostate stage-specific incidence and death rates will be particularly important during future years to ensure a balance is achieved between reducing unnecessary screening and ensuring appropriate and early diagnosis and treatment of more aggressive cases of this important cancer among men.

Despite the successful reductions in the occurrence of and deaths from the most common cancers, several cancer sites show unfavorable trends, particularly liver cancer. Liver cancer death rates are increasing at the highest rate

of all cancer sites among both men and women. Indeed, the incidence of liver cancer is also increasing at rates second only to those of thyroid cancer. The differences in liver cancer incidence observed by sex, race or ethnicity, and birth cohort highlighted in this annual report suggest differences in the distribution of a variety of risk factors among different groups and over time.

HCC is the most common histologic type of primary liver cancer, and HCC trends are largely affected by the changing prevalence of risk factors. In the United States, a critical risk factor is HCV infection.⁷³ Risks for HCV transmission are primarily associated with parenteral exposures, including receipt of contaminated blood and injection drug use. The incidence of HCV infection was highest during the 1960s to 1980s, before the virus was discovered and preventive measures, including HCV screening of the blood supply, became possible. Consequently, the prevalence of HCV infection is particularly high among individuals born during 1945 through 1965.^{28,74,75} Thus, in 2012, the CDC recommended 1-time HCV testing for individuals born during 1945 through 1965 (ages 47-67 years in 2012).³¹ The following year, the USPSTF issued similar recommendations.⁷⁶

This annual report provides evidence of an increased burden of HCV and liver cancer-associated mortality among this birth cohort; although, according to the 2013 National Health Interview Survey, only 12.3% of persons born during 1945 through 1965 reported HCV testing.⁷⁷ Increased liver cancer incidence among this birth cohort is particularly elevated for NH whites, NH blacks, and Hispanics. Findings of a high burden of HCC among certain racial or ethnic groups is consistent with race-specific HCV infection prevalence estimates from US surveys.⁷⁸

Among APIs, HBV is the dominant HCC-related virus, particularly among those not born in the United States.⁷⁹ Because hepatitis B vaccination of infants is now widespread, the prevalence of HBV infection is declining in most Asian countries among vaccinated cohorts of children and adolescents.^{80,81} Accordingly, hepatitis B vaccination is considered a *best buy* for liver cancer prevention.⁸² Consequently, HBV-related HCC among APIs may decline in coming generations. However, in the immediate term, HBV infection prevalence remains high among unvaccinated adults from these countries, representing an ongoing risk of liver cancer.⁸³ HBV testing followed by HBV therapy is associated with a reduction from 50% to 80% in the risk of liver cancer.^{84,85} In 2008, the CDC recommended HBV testing for persons born in sub-Saharan Africa, Asia, and countries in other world regions where HBV infection prevalence is $\geq 2\%$. In 2014, the USPSTF also recommended HBV testing for these target populations.⁸⁶

Cirrhosis is a precursor for most liver cancers. Screening of individuals at risk of cirrhosis increases the chance of detecting liver cancer at an early stage when it is more amenable to therapy. Population groups at risk of cirrhosis include persons with metabolic disease, history of liver disease, history of heavy alcohol use, exposure to HCV or HBV, and some rare genetic disorders.⁸⁷ Increasing evidence suggests that other risk factors, such as type 2 diabetes mellitus and metabolic syndrome (ie, clustering of at least 3 of the following: obesity, elevated blood pressure, elevated fasting plasma glucose, high serum triglycerides, and low high-density lipoprotein levels), are also important contributing factors, particularly when considering the prevalence of these types of medical conditions among the population by using the calculation of a population-attributable fraction (PAF).³² A recent SEER-Medicare analysis of HCC cases diagnosed during 1994 through 2007 among persons aged ≥ 68 years examined odds ratios (ORs) as well as PAFs for the most common risk factors for HCC.³² Among this study population, the strongest predictors of HCC were HCV

infection (OR, 39.9), HBV infection (OR, 11.2), alcohol-related disease (OR, 4.1), metabolic disease (OR, 3.5), and diabetes and/or obesity (OR, 2.3). However, when the prevalence of each risk factor was considered, diabetes and/or obesity had the highest PAF (36.6%), followed by alcohol-related disease (PAF, 23.5%), HCV infection (PAF, 22.4%), HBV infection (PAF, 6.3%), and metabolic disease (PAF, 3.2%).

Although there are a variety of risk factors for liver cancer, approximately 22% of HCC among those aged ≥ 65 years in the United States is attributed to HCV,³² and an estimated 1.6 million persons will be eligible for HCV treatment by 2020.⁸⁸ Previous interferon-based therapies are associated with considerable toxicity,⁸⁹ yet current standards of HCV treatment include from 8 to 12 weeks of all-oral medications with fewer side effects, which can produce a sustained virologic response in $>85\%$ of HCV-infected individuals who complete treatment.⁹⁰⁻⁹² It is estimated that, compared with interferon-based therapy, newer antiviral therapies, such as sofosbuvir-ledipasvir, could prevent an additional 310 cases of HCC per 10,000 treated HCV cases. However, fewer than half of persons living with HCV are aware of their infection; and, among those who know their status, many do not receive appropriate clinical management of HCV infection and associated liver disease.⁹³ Although drug expenditures for treatment of HCV infection have declined as a result of mandated rebates for Medicaid and privately negotiated prices by health plans, the cost of HCV medications may limit the number of patients receiving recommended antiviral therapy.⁹⁴ Barriers to HCV testing and access to adequate care with affordable medications must be overcome to prevent HCV-related liver cancer.⁹⁵

The burden of liver cancer is not equally distributed across the US population, reflecting the heterogeneous prevalence of liver cancer risk factors among groups. Men have nearly a 3-fold higher rate of liver cancer incidence than women. Liver cancer incidence rates generally increase with age. Historically, APIs have been the racial group most affected by liver cancer; however, that may change if the decreasing trend in this group continues as trends increase for other racial groups. Indeed, our analysis indicates that, among individuals ages 55 to 64 years, NH blacks and Hispanics had higher rates than APIs. NH black and Hispanic men have the youngest median age at liver cancer death and the highest APYLL to liver cancer. Although NH whites have lower liver cancer rates than other racial or ethnic groups, they make up a large

segment of the US population and account for the majority of deaths and PYLL to liver cancer in the United States.

Limitations

The completeness, quality, and geographic coverage of cancer incidence data exceed those available for other chronic diseases. The NPCR and SEER data set used for general trends is the most complete and current data set available, covering the vast majority of the US population. However, as with any surveillance data set, local level variations in data quality, incomplete geographic or population reporting, and the complexity of estimating the underlying populations at risk may have influenced the results reported here. For instance, reporting from smaller hospitals or providers unaffiliated with a cancer center may be less complete or may have a longer lag in reporting time. Corrections for late reporting were incorporated into the rates and trends that included delay adjustment; however, this adjustment was not possible for data used to estimate race-specific or ethnicity-specific incidence trends, and differing results may occur, particularly for sites typically diagnosed in a physician's office, like melanoma.

Another issue is the compatibility of the cancer data and the population data by race. Since 2000, the US Census has provided the opportunity for respondents to self-select multiple race categories, which has created incompatibility between the classification of race in the population denominators from the Census (self-reported) with the incidence numerators from registry data (from medical record) and the mortality numerators from the National Vital Statistics System (recorded by medical examiner). The methods for developing single-race estimates from these data are complex and can create additional uncertainties in racial estimates and resultant rates.^{96,97} The broad Hispanic and API categories may mask important epidemiologic variation in risk by country of origin.^{98,99}

We present rates by race separately from Hispanic ethnicity for the cancer incidence and mortality section (Tables 1–4), so the race categories include Hispanics. Thus, as the proportion of the Hispanic population in the United States increases over time, this may influence the reported trends. Shifts in demographics can influence surveillance trends, and our results must be interpreted with this in mind. Furthermore, death rates for the AI/AN, API, and Hispanic populations may be underestimated because of reporting problems on the death certificate and should be interpreted with caution.¹⁰⁰

Long-term trends were reported on the basis of SEER-13 registries, which represent only 14% of the US

population, and the liver cancer incidence-based mortality analysis was based on SEER-18 registries, which represent approximately 28% of the US population. Thus, these analyses may be influenced by the population composition of the SEER areas. More geographic population coverage was available for 5-year and 10-year trends using the combined NPCR and SEER data; however, because of data quality concerns, data from 5 states were excluded from 10-year trends (resulting in 92% coverage), and data from 2 states were excluded for 5-year trends (resulting in 97% coverage), which may influence reported trends. However, >90% of the United States was represented; therefore, these exclusions likely have only a minor effect on national trends.

The limitations of mortality data include the incomplete ascertainment of cases, misclassification, and missing causes of death.^{101,102} However, these biases may be mitigated by analyzing trends in which the problems have been assumed to be relatively constant over time.^{53,103} Finally, despite using the largest national data set available for cancer rates, small numbers for less common sites were an issue for the smaller racial categories, especially AI/AN. Small numbers raise statistical issues, particularly random variation. When evaluating trends, it is vital to assess the magnitude and direction along with the notation of statistical significance, particularly for smaller subgroups.

Future Directions

This annual report brings attention to the growing burden of liver cancer in the United States. Most cases of liver cancer are preventable.¹⁰⁴ One of the most important and preventable risk factors for liver cancer is chronic HCV infection; yet, despite this knowledge, new HCV infections continue to occur.^{28,105} Prevention strategies aimed at reducing the frequency of behaviors that increase the risk of HCV transmission can be effective in reducing HCV infection. Early diagnosis of HCV infection with referral to treatment services can decrease a patient's risk for subsequent health outcomes, such as liver cancer, and can decrease transmission of the virus to others. Cures of HCV infection are associated with a 75% reduction in the risk of liver cancer.^{106,107} In addition to appropriate medical care and management for HCV infection, other strategies to reduce the burden of liver cancer in the United States include promoting hepatitis B vaccination strategies; reducing unhealthy behaviors, such as tobacco use and excessive alcohol use; and reducing obesity by promoting healthy eating and physical activity. Furthermore, improvements in the public health surveillance of both acute and chronic viral hepatitis infections can help to

better monitor the incidence and prevalence of infections and to evaluate interventions.

Although increases in liver cancer incidence and mortality are concerning, the continuing decline in cancer death rates for all sites combined and for the leading cancer sites overall demonstrate progress in cancer prevention and control in general. However, even if incidence rates remain stable or decline, the number of individuals diagnosed with cancer and living after a diagnosis will continue to rise because of improvements in treatment and because of population growth and aging.¹⁰⁸ Thus, primary, secondary, and tertiary cancer prevention efforts at the patient and population-based levels are important. Continued focus on primary prevention efforts to reduce or eradicate risk factors before cancer occurs is critical. Cancer is a heterogeneous disease, and each cancer site has a unique set of risk factors. However, many modifiable cancer risk factors contribute to the burden of many cancer sites, including tobacco use, excess alcohol consumption, poor diet, excess body weight, and physical inactivity.^{109,110} Reductions in these unhealthy behaviors and improvements in healthy lifestyles over time can reduce the burden of cancer.

Although many cancer risk factors are modifiable or avoidable, many are not. Much of the morbidity and mortality associated with cancer can be prevented by detecting the disease at an early stage, when treatment is more effective.^{30,57,111,112} On the basis of systematic reviews of the net benefits and harms of screening, the USPSTF currently recommends population-based screening for colorectal, female breast, and cervical cancers among persons at average risk of developing these cancers and for lung cancer among persons at high-risk on the basis of their cigarette smoking history and age.¹¹³ Regardless of how the cancer is diagnosed, reducing morbidity and mortality associated with the disease depends on timely and appropriate treatment. Removing barriers to receipt of appropriate cancer screening and treatment, including financial barriers, is crucial.¹¹⁴ Programs like the CDC's National Breast and Cervical Cancer Early Detection Program⁶⁶ and the CDC's Colorectal Cancer Control Program⁶³ can provide needed services, such as free or low-cost early cancer detection examinations, patient navigation services, and treatment.

For individuals diagnosed with cancer (cancer survivors), methods to mitigate the negative effects of a diagnosis and its treatment and to prevent the recurrence of cancer are also critical. Cancer survivors often face long-term adverse physical, psychosocial, and financial effects from their cancer diagnosis and treatment.¹¹⁵⁻¹²¹ In addition,

cancer survivors are at an increased risk of subsequent primary cancers.^{122,123} Cancer can have a long-term impact on the health and well being of the cancer survivor. This has important implications for ongoing preventive care for all cancers and comorbid conditions.

Finally, disease surveillance is essential to the practice of public health for guiding prevention and control activities, monitoring trends, and evaluating outcomes.^{124,125} Information obtained from cancer incidence registries and vital statistics systems provide decision makers with vital information necessary to lead and manage effective cancer prevention and control programs. Cancer registry systems are among the most sophisticated and standardized surveillance systems in the United States. Routine monitoring of cancer incidence and mortality helps to evaluate outcomes of public health-oriented cancer prevention efforts and to identify areas and populations with high cancer incidence or mortality rates that can benefit from targeted interventions to promote healthy environments and behaviors.

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