

Annual Report to the Nation on the Status of Cancer, 1975-2006, Featuring Colorectal Cancer Trends and Impact of Interventions (Risk Factors, Screening, and Treatment) to Reduce Future Rates

Brenda K. Edwards, PhD¹; Elizabeth Ward, PhD²; Betsy A. Kohler, MPH, CTR³; Christie Ehemann, PhD⁴; Ann G. Zauber, PhD⁵; Robert N. Anderson, PhD⁶; Ahmedin Jemal, DVM, PhD²; Maria J. Schymura, PhD^{3,7}; Iris Lansdorp-Vogelaar, MS, PhD⁸; Laura C. Seeff, MD⁴; Marjolein van Ballegooijen, MD, PhD⁸; S. Luuk Goede, MSc⁸; and Lynn A. G. Ries, MS¹

BACKGROUND. The American Cancer Society, the Centers for Disease Control and Prevention (CDC), the National Cancer Institute (NCI), and the North American Association of Central Cancer Registries (NAACCR) collaborate annually to provide updated information regarding cancer occurrence and trends in the United States. This year's report includes trends in colorectal cancer (CRC) incidence and death rates and highlights the use of microsimulation modeling as a tool for interpreting past trends and projecting future trends to assist in cancer control planning and policy decisions. **METHODS.** Information regarding invasive cancers was obtained from the NCI, CDC, and NAACCR; and information on deaths was obtained from the CDC's National Center for Health Statistics. Annual percentage changes in the age-standardized incidence and death rates (based on the year 2000 US population standard) for all cancers combined and

Corresponding author: Brenda K. Edwards, PhD, Surveillance Research Program, National Cancer Institute, 6116 Executive Boulevard, Bethesda, MD 20892-8315; Fax: (301) 480-4077; edwardsb@mail.nih.gov

¹Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, Maryland; ²Surveillance and Health Policy Research Department, American Cancer Society, Atlanta, Georgia; ³North American Association of Central Cancer Registries, Springfield, Illinois; ⁴Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; ⁵Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, New York; ⁶Division of Vital Statistics, National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, Maryland; ⁷New York State Cancer Registry, Menands, New York; ⁸Department of Public Health, Erasmus Medical Center, University Medical Center Rotterdam, the Netherlands

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official positions of the Centers for Disease Control and Prevention.

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for the top 15 cancers were estimated by joinpoint analysis of long-term trends (1975-2006) and for short-term fixed-interval trends (1997-2006). All statistical tests were 2-sided. **RESULTS.** Both incidence and death rates from all cancers combined significantly declined ($P < .05$) in the most recent time period for men and women overall and for most racial and ethnic populations. These decreases were driven largely by declines in both incidence and death rates for the 3 most common cancers in men (ie, lung and prostate cancers and CRC) and for 2 of the 3 leading cancers in women (ie, breast cancer and CRC). The long-term trends for lung cancer mortality in women had smaller and smaller increases until 2003, when there was a change to a nonsignificant decline. Microsimulation modeling demonstrates that declines in CRC death rates are consistent with a relatively large contribution from screening and with a smaller but demonstrable impact of risk factor reductions and improved treatments. These declines are projected to continue if risk factor modification, screening, and treatment remain at current rates, but they could be accelerated further with favorable trends in risk factors and higher utilization of screening and optimal treatment. **CONCLUSIONS.** Although the decrease in overall cancer incidence and death rates is encouraging, rising incidence and mortality for some cancers are of concern. *Cancer* 2010;000:000-000. © 2009 American Cancer Society.

KEYWORDS: cancer, incidence, mortality, Surveillance, Epidemiology, and End Results, North American Association of Central Cancer Registries, National Program of Cancer Registries, United States, Cancer Intervention and Surveillance Modeling Network colon models, microsimulation models, colorectal cancer.

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) collaborate each year to produce a report to the nation on the current status of cancer in the United States. The first report, published in 1998, documented the first sustained decline in cancer death rates since the 1930s.¹ Subsequent reports have updated information on trends in incidence and death rates and featured in-depth analyses of selected topics,²⁻¹⁰ including incidence and mortality trends for colorectal cancer (CRC).¹¹ The current report provides updated trends in incidence and death rates for all cancers combined and for the top 15 cancers among all races combined and among each of the 5 major racial/ethnic groups (white, black, Asian and Pacific Islander [API], American Indian/Alaska Natives [AI/AN], and Hispanic) by sex; it also provides incidence and mortality data for AI/AN who reside in counties covered by the Indian Health Service (IHS) Contract Health Services Delivery Area (CHSDA). Furthermore, this report provides an update on incidence and mortality trends for CRC and uses a microsimulation model of CRC to interpret past trends and project future trends. Our application of simulation modeling provides information on the relative impact of modifiable risk factors, screening use, and treatment patterns on cancer trends and compares different future scenarios. The meth-

odology did not focus on applications comparing multiple strategies for a category of interventions (eg, screening tests) nor multiple types of models. The report also highlights the use of microsimulation models to assist in cancer prevention and control planning and in setting public policy (available at: <http://cisnet.cancer.gov/projections/colorectal/> accessed on September 30, 2009).

MATERIALS AND METHODS

Cancers, Cancer Deaths, and Population Estimates

Information on newly diagnosed invasive cancers, including in situ cancers of the bladder, was obtained from population-based cancer registries that participate in the NCI's Surveillance, Epidemiology, and End Results (SEER) Program and/or the CDC's National Program of Cancer Registries (NPCR). All participating cancer registries are members of the NAACCR.

Site and histology for incidence cancers were coded according to the International Classification of Diseases (ICD) for Oncology (ICD-O) edition in use at the time of diagnosis, converted to the third edition coding,¹² and categorized according to SEER site groups.¹³ For cancer deaths, the underlying causes of death were selected according to the version of the ICD codes and selection

rules in use at the time of death (ICD-6 through ICD-10).¹⁴⁻¹⁸

Cause of death is based on death certificate information reported to state vital statistics offices; this information is consolidated through the CDC National Center for Health Statistics (NCHS) National Vital Statistics System¹⁹ and categorized according to SEER anatomic site groups¹³ to maximize comparability among ICD and ICD-O versions. County-level population estimates, summed to the state and national level, were used as denominators in rate calculations.²⁰ Because the 2000 US census allowed respondents to identify themselves as multiracial, the NCHS and the Census Bureau developed methods for bridging multiple-race population estimates to single-race estimates to describe long-term trends in disease rates by race.²¹ The Census Bureau has provided NCI with bridged, single-race annual population estimates from 1990-2007 with annual re-estimates calculated back to the most recent decennial census. NCI makes slight modifications to the Hawaii population estimates based on additional local information (available at: <http://seer.cancer.gov/popdata/methods.html> accessed on August 21, 2009).

For most states, population estimates as of July 1 of each year were used to calculate annual incidence and death rates, because these estimates are presumed to reflect the average population of a defined geographic area for a calendar year. For Louisiana, Alabama, Mississippi, and Texas, where residents were displaced in the fall of 2005 by hurricanes Katrina and Rita, incidence data for the first 6 months of 2005 and half of the July 1 population estimate were used to calculate state-specific incidence rates for 2005. For the 2005 death rate calculations, the NCI made adjustments to the 2005 population estimates to account for the displacement, and these data were made available for use by the cancer surveillance agencies. The national total population estimates are not affected by these adjustments. Further details on these calculations are provided at <http://seer.cancer.gov/popdata/methods.html> (accessed on August 21, 2009).

Incidence data are not available uniformly for every period, geographic area, or racial and ethnic group in the United States. Therefore, analyses of long-term (1975-2006) and short-term fixed-interval (1997-2006) trends in incidence rates and in 5-year (2002-2006) average age-standardized incidence rates for the top 15

cancer sites include different geographic areas and populations. To evaluate the long-term incidence trends (1975-2006) for all races and ethnicities combined, data were used from the 9 original SEER areas (Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah), which cover approximately 10% of the US population (9% each of US whites and US blacks, 8% of US Hispanics, and 19% of US Asians).²² Data from 33 population-based cancer registries were used to assess short-term trends (1997-2006), and data from 43 population-based cancer registries were used to estimate 5-year average annual (2002-2006), age-standardized incidence rates for all races and ethnicities combined and for each of the 5 major racial/ethnic populations (white, black, API, AI/AN residing in counties covered by the IHS CHSDA, and Hispanic). The 33 and 43 registries met NAACCR's data-quality criteria for every year that was included in the analysis; these registries cover approximately 71% and 86% of the US population, respectively. The 33 cancer registries cover 71% of the US white population, 63% of the US black population, 88% of the US Hispanic population, 87% of the US API population, and 72% of the AI/AN (CHSDA) population; the 43 cancer registries cover 86% of the US white population, 83% of the US black population, 92% of the US Hispanic population, 93% of the US API population, and 78% of the US AI/AN (CHSDA) population. New incidence cases identified through the IHS were incorporated into the pooled cancer registry analysis file.⁹

US mortality data from NCHS were unavailable for every racial/ethnic group for all periods studied; notably, the Hispanic ethnicity was not reported on death certificates in every state for all years during the period 1997-2006. For all races and ethnicities combined, we examined long-term (1975-2006) trends, short-term (1997-2006) trends, and 5-year (2002-2006) average annual age-standardized death rates for all cancer sites and for the top 15 cancer sites for men and women in each of the 5 major racial/ethnic populations (white, black, API, AI/AN CHSDA, and Hispanic). Mortality data for the AI/AN population were based on deaths in counties served by IHS's CHSDA, because estimated rates based on CHSDA counties reportedly are more reliable than national data.⁹

Statistical Analysis

Age-specific and age-standardized rates were expressed per 100,000 population (based on the year 2000 US standard population) and were generated by using SEER*Stat Software, version 6.5.2 (available at: <http://www.seer.cancer.gov/seerstat>²³ and <http://seer.cancer.gov/popdata/methods.html> accessed on August 21, 2009). Rates for 2002-2006 were suppressed if the numerator was <16 observations, consistent with our previous work.⁶⁻¹⁰

Long-term trends (1975-2006) in age-standardized SEER 9 cancer incidence and US death rates were described using joinpoint regression analysis, which involves fitting a series of joined straight lines on a logarithmic scale to the trends in the annual age-standardized rates (available at: http://seer.cancer.gov/csr/1975_2006/technotes/joinpoint.html accessed on September 15, 2009). We allowed a maximum of 4 joinpoints in the model to better characterize emerging trends, which are expressed in up to 5 variable time intervals. The method is described in detail elsewhere.²⁴ The resulting trends of various time periods are described by the annual percent change (APC) (ie, the slope of the line segment).²⁴ Long-term incidence trends are based on both observed data and data adjusted for reporting delay (which mostly affects recent years).²⁵ Our descriptions of long-term trends in incidence are based on the delay-adjusted data except when specifically noted. For short-term, fixed-interval (1997-2006) trend analyses, a joinpoint regression analysis with a maximum of 1 joinpoint was used to estimate APCs.

This year's report provides the average APC (AAPC) as an addendum to the underlying joinpoint trends and as a summary measure to compare fixed-interval trends by race/ethnicity. The AAPC quantifies the average trend over a period of multiple years. It can be estimated even if the joinpoint model indicates that changes in trends occurred during those years, because the AAPC is estimated as a geometric weighted average of the joinpoint APCs, with the weights equal to the lengths of each segment over the pre-specified fixed interval (available at: <http://srab.cancer.gov/joinpoint/aapc.html> accessed on September 15, 2009).^{26,27} The APC was suppressed if the numerator was <10 cancers for any year within the designated time interval, consistent with our previous methods.⁶⁻¹⁰

In describing long-term and short-term trends with estimates of APC and AAPC, the terms "increase" and

"decrease" were used when the slope (APC or AAPC) of the trend was statistically significant ($P < .05$). When the trend was not significant, terms such as "level," "stable," "nonsignificant increase," and "nonsignificant decrease" were used, depending on the results.

CRC Rates and Trends

Age-standardized CRC incidence rates for diagnosis years 2002-2006 and AAPC estimates of short-term trends for diagnosis years 1997-2006 were based on SEER and NPCR pooled data reported by the NAACCR. For diagnosis years 2002-2006, we also present 5-year average age-specific CRC incidence rates for groups aged <50 years, aged 50-64 years, and aged ≥ 65 years; for colorectal subsites (proximal colon, distal colon, rectum, and other); for racial/ethnic groups (white, black, API, AI/AN CHSDA, Hispanic, and non-Hispanic); and for combinations of these variables. Anatomic subsite was based on the ICD-O-3 codes for broad categories: proximal colon (codes C18.0 and C18.2-C18.5), distal colon (codes C18.6 and C18.7), rectum (codes C19.9 and C20.9), and other (codes C18.1, C18.8, C18.9, and C26.0). Changes in coding rules for stage of cancer at diagnosis, particularly introduction of the Collaborative Stage (CS) Data Collection System (available at: <http://training.seer.cancer.gov/collaborative> accessed on September 30, 2009) for cases diagnosed in 2004 forward, caused a systematic shift in stage between 2003 and 2004 and, thus, precluded the use of NAACCR pooled data to evaluate stage-specific cancer incidence trends. Stage-specific analyses were based on the SEER Extent of Disease codes and CS for the SEER 9 registries (available at: <http://seer.cancer.gov> accessed on September 30, 2009). Long-term trends in stage-specific incidence rates and 5-year stage-specific relative survival for CRC used the SEER 9 data for diagnosis years 1975-2006, based on historic stage (localized, regional, distant, and unknown).

CRC Incidence and Mortality Models: Assessing the Impact of Risk Factors, Screening, and Treatment

We used a microsimulation model,²⁸ microsimulation screening analysis (MISCAN-Colon), from NCI's Cancer Intervention and Surveillance Modeling Network (CISNET) consortium (available at: <http://cisnet.cancer.gov/>

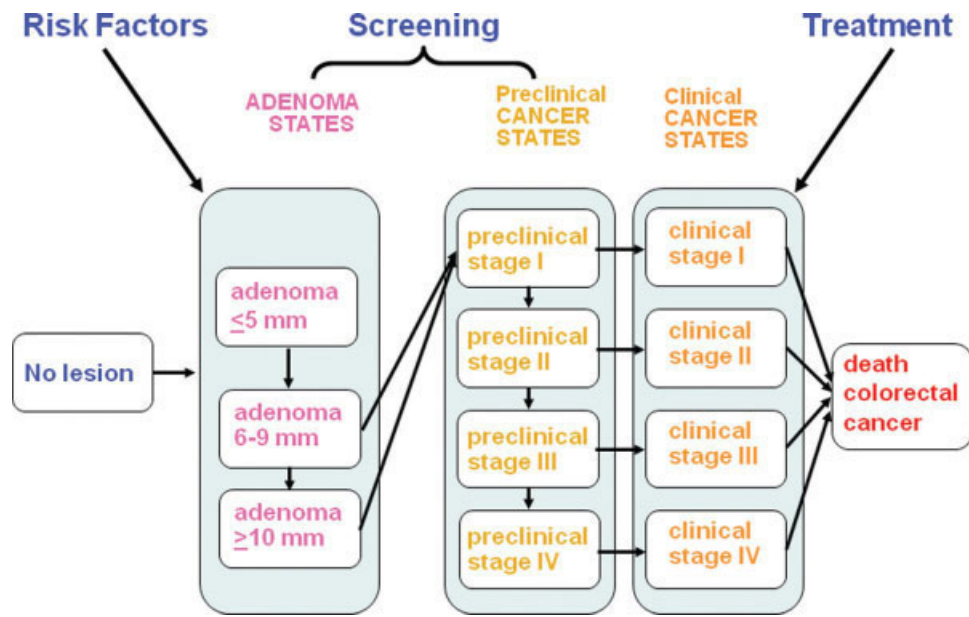


Figure 1. This is a graphic representation of the adenoma-carcinoma sequence in the microsimulation screening analysis (MISCAN-Colon) model and potential interventions that affect the natural history of disease. The natural history of colorectal cancer is depicted from adenoma to carcinoma. An individual can develop 1 or more adenomas, which can increase in size. Some adenomas will become invasive cancers, which initially are preclinical and then become clinical. The opportunity to intervene in the natural history through risk factors, screening, and treatment is noted.

projections/colorectal accessed on September 30, 2009) to estimate the impact of historic changes in risk factors, screening, and treatment on past CRC incidence and mortality trends and to project future mortality trends through 2020. The projections of future mortality trends have been published previously, whereas the past trends are an intermediate result of this previously published work. Consequently, the model methodology, inputs, and assumptions have been described previously.²⁹⁻³¹ Briefly, the MISCAN-Colon model simulates the US population from 1975 to 2020 based on the sequence of developments as an adenoma becomes cancer.³²⁻³⁴ The model also distinguishes 3 types of interventions that are considered separately and as combined interventions that can affect the natural history of the adenoma-carcinoma sequence (Fig. 1).^{29,35,36} MISCAN-Colon models the influence of risk factors through changing the risk of developing adenomas. Screening is modeled as potentially affecting adenomas, preclinical disease, and clinical disease (the effect depends on the screening test).

The MISCAN-Colon model includes risk factors that can increase risk for CRC (eg, smoking, obesity, and red meat consumption) and factors that may decrease risk for CRC (eg, aspirin use, multivitamin use [including supplemental folate and calcium], and physical activity).

We modeled the impact of the risk factors by using the relative risk for adenomas associated with each factor in conjunction with the prevalence of the factor over time in the population, as described previously²⁹ (available at: <http://cisnet.cancer.gov/projections/colorectal> accessed on September 30, 2009). Prevalence rates were obtained primarily from the Cancer Progress Report.³⁷ We assumed a smoking rate of 42% in 1965, 23% in 2000, and a projected rate of 11% to 17% in 2020, depending on the future scenario. We assumed an obesity rate of 13% in 1965, 31% in 2000, and a projected rate of 34% to 45% in 2020. For CRC screening uptake, we used National Health Interview Survey (NHIS)³⁸ data from 1987, 1992, 1998, and 2000 to estimate screening test rates for fecal occult blood testing (FOBT) for individuals aged ≥ 50 years who have had an FOBT within past 2 years and endoscopy (including flexible sigmoidoscopy and colonoscopy) for individuals aged ≥ 50 years who have had a sigmoidoscopy or colonoscopy (collectively known as endoscopy) at some point in their life, by 5-year age groups, and applied both screening rates and the sensitivity and specificity of each screening test to the model. CRC screening rates by 5-year age groups were calculated separately for home-based FOBT and endoscopy (including flexible sigmoidoscopy and colonoscopy). The NHIS

Table 1. Surveillance, Epidemiology, and End Results Cancer Incidence Rate Trends With Joinpoint Analyses for 1975-2006 for the Top 15 Cancers, by Sex, for All Races^a

Sex/Cancer Site or Type	Joinpoint Analyses (1975-2006) ^b											
	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		AAPC ^f	
	Years	APC ^e	Years	APC ^e	Years	APC ^e	Years	APC ^e	Years	APC ^e	1997-2006	2002-2006
All sites^c												
Both sexes	1975-1989	1.2 ^g	1989-1992	2.8 ^g	1992-1995	-2.4	1995-1999	1.0	1999-2006	-1.1 ^g	-0.6 ^h	-1.1 ^h
(Delay-adjusted)	1975-1989	1.2 ^g	1989-1992	2.8	1992-1995	-2.4	1995-1999	0.9	1999-2006	-0.7 ^g	-0.4 ^h	-0.7 ^h
Males	1975-1989	1.3 ^g	1989-1992	5.1 ^g	1992-1995	-4.8 ^g	1995-2001	0.3	2001-2006	-1.9 ^g	-0.9 ^h	-1.9 ^h
(Delay-adjusted)	1975-1989	1.3 ^g	1989-1992	5.2 ^g	1992-1995	-4.9 ^g	1995-2000	0.5	2000-2006	-1.3 ^g	-0.7 ^h	-1.3 ^h
Females	1975-1979	-0.3	1979-1987	1.6 ^g	1987-1995	0.1	1995-1998	1.5	1998-2006	-0.8 ^g	-0.5 ^h	-0.8 ^h
(Delay-adjusted)	1975-1979	-0.3	1979-1987	1.6 ^g	1987-1995	0.1	1995-1998	1.4	1998-2006	-0.5 ^g	-0.3	-0.5 ^h
Top 15 cancers for males^d												
Prostate	1975-1988	2.6 ^g	1988-1992	16.4 ^g	1992-1995	-11.4 ^g	1995-2001	1.8	2001-2006	-3.4 ^g	-1.1	-3.4 ^h
(Delay-adjusted)	1975-1988	2.6 ^g	1988-1992	16.5 ^g	1992-1995	-11.7 ^g	1995-2000	2.4	2000-2006	-2.4 ^g	-0.8	-2.4 ^h
Lung and bronchus	1975-1982	1.4 ^g	1982-1991	-0.4	1991-2006	-1.9 ^g					-1.9 ^h	-1.9 ^h
(Delay-adjusted)	1975-1982	1.4 ^g	1982-1991	-0.4	1991-2006	-1.8 ^g					-1.8 ^h	-1.8 ^h
Colon and rectum	1975-1986	1.1 ^g	1986-1995	-2.1 ^g	1995-1998	1.1	1998-2004	-2.6 ^g	2004-2006	-5.7 ^g	-2.9 ^g	-4.2 ^h
(Delay-adjusted)	1975-1985	1.1 ^g	1985-1991	-1.2 ^g	1991-1995	-3.2 ^g	1995-1998	2.1	1998-2006	-3.0 ^g	-2.5 ^h	-3.0 ^h
Urinary bladder	1975-1987	1.0 ^g	1987-1996	-0.5	1996-1999	1.8	1999-2006	-0.8 ^g			-0.2	-0.8 ^h
(Delay-adjusted)	1975-1987	0.9 ^g	1987-2006	0.0							0.0	0.0
Melanoma of the skin	1975-1986	5.5 ^g	1986-2006	2.9 ^g							2.9 ^h	2.9 ^h
(Delay-adjusted)	1975-1986	5.4 ^g	1986-2006	3.1 ^g							3.1 ^h	3.1 ^h
Non-Hodgkin lymphoma	1975-1991	4.3 ^g	1991-2006	0.1							0.1	0.1
(Delay-adjusted)	1975-1991	4.2 ^g	1991-2006	0.3							0.3	0.3
Kidney and renal pelvis	1975-2006	1.7 ^g									1.7 ^h	1.7 ^h
(Delay-adjusted)	1975-2006	1.8 ^g									1.8 ^h	1.8 ^h
Leukemia	1975-2004	-0.1	2004-2006	-6.6							-1.6 ^h	-3.4
(Delay-adjusted)	1975-2006	0.1 ^g									0.1 ^h	0.1 ^h
Oral cavity and pharynx	1975-1983	-0.2	1983-2006	-1.4 ^g							-1.4 ^h	-1.4 ^h
(Delay-adjusted)	1975-2006	-1.2 ^g									-1.2 ^h	-1.2 ^h
Pancreas	1975-1993	-0.9 ^g	1993-2006	0.3							0.3	0.3
(Delay-adjusted)	1975-1981	-1.8 ^g	1981-1985	1.1	1985-1990	-2.1	1990-2003	0.1	2003-2006	2.5	0.9	1.9
Stomach	1975-1988	-1.2 ^g	1988-2006	-2.0 ^g							-2.0 ^h	-2.0 ^h
(Delay-adjusted)	1975-1988	-1.2 ^g	1988-2006	-2.0 ^g							-2.0 ^h	-2.0 ^h
Liver and intrahepatic bile duct	1975-1986	2.1 ^g	1986-1996	4.9 ^g	1996-2006	2.6 ^g					2.6 ^h	2.6 ^h
(Delay-adjusted)	1975-2006	3.6 ^g									3.6 ^h	3.6 ^h
Esophagus	1975-2006	0.7 ^g									0.7 ^h	0.7 ^h
(Delay-adjusted)	1975-2006	0.7 ^g									0.7 ^h	0.7 ^h
Brain and other nervous system	1975-1991	1.1 ^g	1991-2006	-0.7 ^g							-0.7 ^h	-0.7 ^h
(Delay-adjusted)	1975-1991	1.0 ^g	1991-2006	-0.5 ^g							-0.5 ^h	-0.5 ^h
Myeloma	1975-2002	0.8 ^g	2002-2006	-3.0							-0.9	-3.0
(Delay-adjusted)	1975-2006	0.7 ^g									0.7 ^h	0.7 ^h
Top 15 cancers for females^d												
Breast	1975-1980	-0.5	1980-1987	4.0 ^g	1987-1994	-0.2	1994-1999	1.6 ^g	1999-2006	-2.2 ^g	-1.3 ^h	-2.2 ^h
(Delay-adjusted)	1975-1980	-0.5	1980-1987	4.0 ^g	1987-1994	-0.1	1994-1999	1.6 ^g	1999-2006	-2.0 ^g	-1.2 ^h	-2.0 ^h
Lung and bronchus	1975-1982	5.5 ^g	1982-1990	3.5 ^g	1990-1998	1.0 ^g	1998-2006	-0.1			0.0	-0.1
(Delay-adjusted)	1975-1982	5.6 ^g	1982-1991	3.4 ^g	1991-2006	0.4 ^g					0.4 ^h	0.4 ^h
Colon and rectum	1975-1985	0.3	1985-1995	-1.9 ^g	1995-1998	2.0	1998-2006	-2.4 ^g			-1.9 ^h	-2.4 ^h
(Delay-adjusted)	1975-1985	0.3	1985-1995	-1.8 ^g	1995-1998	1.9	1998-2006	-2.2 ^g			-1.7 ^h	-2.2 ^h
Corpus and uterus, NOS	1975-1979	-6.0 ^g	1979-1988	-1.7 ^g	1988-1997	0.7 ^g	1997-2006	-0.6 ^g			-0.6 ^h	-0.6 ^h
(Delay-adjusted)	1975-1979	-6.0 ^g	1979-1988	-1.7 ^g	1988-1997	0.7 ^g	1997-2006	-0.5 ^g			-0.5 ^h	-0.5 ^h
Melanoma of the skin	1975-1980	5.6 ^g	1980-2006	2.4 ^g							2.4 ^h	2.4 ^h
(Delay-adjusted)	1975-1981	5.7 ^g	1981-1993	1.9 ^g	1993-2006	3.0 ^g					3.0 ^h	3.0 ^h
Non-Hodgkin lymphoma	1975-1990	2.8 ^g	1990-2004	1.2 ^g	2004-2006	-2.5					0.3	-0.7
(Delay-adjusted)	1975-1990	2.9 ^g	1990-2006	1.1 ^g							1.1 ^h	1.1 ^h

(Continued)

Table 1. (Continued)

Sex/Cancer Site or Type	Joinpoint Analyses (1975-2006) ^b											
	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		AAPC ^f	
	Years	APC ^e	Years	APC ^e	Years	APC ^e	Years	APC ^e	Years	APC ^e	1997-2006	2002-2006
Thyroid	1975-1977	6.5	1977-1980	-5.3	1980-1995	2.3 ^g	1995-2006	6.0 ^g			6.0 ^h	6.0 ^h
(Delay-adjusted)	1975-1977	6.5	1977-1980	-5.3	1980-1995	2.3 ^g	1995-2006	6.3 ^g			6.3 ^h	6.3 ^h
Ovary ^c	1975-1985	0.1	1985-2001	-0.7 ^g	2001-2006	-2.6 ^g					-1.8 ^h	-2.6 ^h
(Delay-adjusted) ^e	1975-1985	0.1	1985-2001	-0.7 ^g	2001-2006	-2.1 ^g					-1.5 ^h	-2.1 ^h
Pancreas	1975-1984	1.5 ^g	1984-1995	-0.6	1995-2006	0.6 ^g					0.6 ^h	0.6 ^h
(Delay-adjusted)	1975-1984	1.3 ^g	1984-2000	-0.3	2000-2006	1.7 ^g					1.0 ^h	1.7 ^h
Leukemia	1975-2006	0.0									0.0	0.0
(Delay-adjusted)	1975-2006	0.3 ^g									0.3 ^h	0.3 ^h
Kidney and renal pelvis	1975-2006	2.3 ^g									2.3 ^h	2.3 ^h
(Delay-adjusted)	1975-2006	2.4 ^g									2.4 ^h	2.4 ^h
Urinary bladder	1975-2003	0.2 ^g	2003-2006	-2.3							-0.6	-1.7
(Delay-adjusted)	1975-2006	0.2 ^g									0.2 ^h	0.2 ^h
Cervix uteri	1975-1981	-4.6 ^g	1981-1996	-1.1 ^g	1996-2006	-3.6 ^g					-3.6 ^h	-3.6 ^h
(Delay-adjusted)	1975-1981	-4.6 ^g	1981-1996	-1.1 ^g	1996-2006	-3.5 ^g					-3.5 ^h	-3.5 ^h
Oral cavity and pharynx	1975-1980	2.6 ^g	1980-2006	-1.0 ^g							-1.0 ^h	-1.0 ^h
(Delay-adjusted)	1975-1980	2.5	1980-2006	-0.9 ^g							-0.9 ^h	-0.9 ^h
Brain and other nervous system	1975-1987	1.6 ^g	1987-2006	-0.3							-0.3	-0.3
(Delay-adjusted)	1975-1987	1.6 ^g	1987-2006	-0.1							-0.1	-0.1

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

^aSource: Surveillance, Epidemiology, and End results (SEER) 9 areas covering about 10% of the U.S. population (Connecticut, Hawaii, Iowa, Utah, and New Mexico, and the metropolitan areas of San Francisco, Detroit, Atlanta, and Seattle-Puget Sound).

^bJoinpoint analyses with up to 4 joinpoints are based on rates per 100,000 persons and were age-adjusted to the 2000 U.S. standard population (19 age groups) using the Joinpoint (JP) Regression Program, version 3.3.1, April 2008, National Cancer Institute.

^cAll sites excludes myelodysplastic syndromes and borderline tumors; ovary excludes borderline tumors.

^dThe top 15 cancers were selected based on the sex-specific, age-adjusted incidence rates for 2002-2006 for all races combined and are listed in rank order.

^eThe APC is based on rates that were age-adjusted to the 2000 U.S. standard population (19 age groups).

^fThe AAPC is a weighted average of the APCs calculated by Joinpoint.

^gThe APC is statistically significantly different from zero (2-sided $P < .05$).

^hThe AAPC is statistically significantly different from zero.

did not distinguish between home-based FOBT and office-based FOBT or the type of endoscopy before the 2000 survey. Because office-based FOBT is not an effective method for CRC screening,³⁹ the proportion of home-based FOBT in 2000 was applied to the earlier years of data to calculate FOBT prevalence. Similarly, the proportions of endoscopies that were sigmoidoscopies and colonoscopies were derived from the 2000 data and applied to earlier years. For 2000, we assumed a CRC screening rate of 24% with FOBT and 39% for endoscopy and a projected increase in screening rates in 2020, with an FOBT prevalence of 35% to 38% and an endoscopy prevalence of 56% to 61% (see Supporting Information Table 1; available at: www.seer.cancer.gov/report_to_nation/1975-2006). We assumed no CRC screening before 1978.

To assess the effects of treatment, the model distinguished 4 chemotherapy regimens for stage III-IV CRC,

depending on the treatment available to US patients diagnosed in different periods. These regimens were 1) 5-fluorouracil (5-FU) (available before 1996); 2) 5-fluorouracil and irinotecan (available 1996-2001); 3) 5-FU, irinotecan, and oxaliplatin (2002-2003); and 4) 5-FU, irinotecan, oxaliplatin, and bevacizumab/cetuximab (2004 and afterward). Hazard ratios for disease-free survival were obtained from published clinical trials for each of the treatment regimens⁴⁰⁻⁵² and were applied to the 1975 through 1979 stage-specific relative survival rates from SEER 9. Chemotherapy use by age and time for the US population were based on the SEER-Medicare linked database,⁵³ survey data, and patterns of care studies.^{54,55} We assumed increasing CRC treatment rates over time, with a projected rate of 8% in 2005 and that, by 2020, 45% to 83% of patients with CRC would be treated with combination therapy, including 5-FU, irinotecan, oxaliplatin, and biologics.

The key long-term outcomes measured in the MIS-CAN-Colon model are the changes in CRC incidence and death rates as a result of the changes in risk factors, screening, and treatment in past and future time periods. To project future trends,²⁹ we considered 3 hypothetical scenarios, including frozen trends (risk factor, screening, and treatment rates plateau at year 2000), continued trends (risk factor, screening, and treatment rates continue to increase annually at the current rate), and optimistic trends, in which all 3 interventions of risk factors, screening, and treatment improved at a rate that was considered optimistic but realistic.²⁹ The prevalence assumptions of these factors from 1965 to 2000, as observed, and from 2000 to 2020, as projected under each scenario, are presented online at www.seer.cancer.gov/report_to_nation/1975-2006 in Supporting Information Table 1 and in previous work.²⁹

RESULTS

Long-Term Incidence Trends for All Races Combined, 1975-2006

Overall cancer incidence rates for all racial/ethnic groups combined decreased by 0.7% per year during 1999-2006 for both sexes combined, by 1.3% per year during 2000-2006 for men, and by 0.5% per year during 1998-2006 for women (Table 1). Trends during the most recent periods (last joinpoint segments), along with AAPCs for the most recent 5 years (2002-2006) and 10 years (1997-2006), are presented for the top 15 cancers by sex. Among men, rates decreased for cancers of the prostate, lung and bronchus (lung), oral cavity and pharynx (oral cavity), stomach, brain and other nervous system (brain), and for CRC. In contrast, rates increased for cancers of the kidney and renal pelvis (kidney), liver and intrahepatic bile duct (liver), and esophagus and for leukemia, myeloma, and melanoma of the skin (melanoma). Among women, incidence rates decreased during the most recent joinpoint segments for 6 of the top 15 cancers (ie, breast, CRC, uterine corpus and uterus not otherwise specified [uterus], ovary, cervix uteri [cervix], and oral cavity). In contrast, rates increased for 8 of the top 15 cancers (ie, lung, thyroid, pancreas, urinary bladder [bladder], kidney, non-Hodgkin lymphoma [NHL], melanoma, and leukemia) in women.

On the basis of long-term trends (1975-2006), the AAPCs for the most recent 5 years, 2002-2006, were simi-

lar to the APCs for the most recent joinpoint segment (time period) (Table 1). When the incidence trend fluctuated over time, as expected, the 10-year (1997-2006) AAPCs differed from the most recent APCs (eg, all sites combined for men and women; cancers of the prostate, pancreas, and CRC in men; and cancers of the breast, pancreas, uterus, and CRC in women). Specifically, the 10-year AAPC (1997-2006) for prostate cancer had a small, nonsignificant decrease that reflected a nonsignificant increase during 1995-2000 attenuated by a more recent, significant 2.4% decline observed over the period 2000-2006. Similarly, breast cancer incidence in women began to decline at the turn of the century after an increase in the latter part of the 1990s (1994-1999). The 10-year breast cancer AAPC for 1997-2006 was a smaller decline of 1.2% per year rather than the more recent annual decrease of 2.0% each year over the period 1999-2006.

Long-Term Mortality Trends for All Races Combined, 1975-2006

Death rates for all cancers combined have decreased since the early 1990s for both men and women (Table 2). The decreases were slightly larger for men, who had declines of 1.5% per year during 1993-2001 and 2.0% per year during 2001-2006 compared with women, whose cancer death rates declined 0.8% per year during 1994-2002 and 1.5% per year during 2002-2006. Among the top 15 leading causes of cancer death, mortality decreased during the most recent period for the following sites: CRC, stomach, kidney, brain, leukemia, NHL, and myeloma in both men and women; lung, prostate, and oral cavity in men; and breast, ovary, and bladder in women. Cancers with increasing mortality during the most recent period include melanoma and esophageal cancer in men, pancreatic cancer in women, and liver cancer in both men and women.

Similar to incidence trends, the AAPCs in death rates for 2002-2006 generally were similar to the APCs for the most recent joinpoint period. However, the use of long-term trends often can mask changes over the shorter term. Differences in the 5-year and 10-year AAPCs typically identify types of cancer in which the 10-year trend may mask important recent changes. Some examples are the accelerated rate of decline for CRC mortality for men and for women and the recent shift toward increasing mortality in melanoma among men.

Table 2. U.S. Death Rate Trends With Joinpoint Analyses for 1975-2006 for the Top 15 Cancers, by Sex, for All Races^a

Sex/cancer site or type	Joinpoint Analyses (1975-2006) ^b										AAPC ^e	
	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		1997-2006	2002-2006
	Years	APC ^d	Years	APC ^d	Years	APC ^d	Years	APC ^d	Years	APC ^d		
All sites												
Both sexes	1975-1990	0.5 ^f	1990-1993	-0.3	1993-2001	-1.1 ^f	2001-2006	-1.6 ^f			-1.4 ^g	-1.6 ^g
Males	1975-1979	1.0 ^f	1979-1990	0.3 ^f	1990-1993	-0.5	1993-2001	-1.5 ^f	2001-2006	-2.0 ^f	-1.8 ^g	-2.0 ^g
Females	1975-1990	0.6 ^f	1990-1994	-0.1	1994-2002	-0.8 ^f	2002-2006	-1.5 ^f			-1.1 ^g	-1.5 ^g
Top 15 cancers for males^c												
Lung and bronchus	1975-1978	2.5 ^f	1978-1984	1.2 ^f	1984-1990	0.4 ^f	1990-1994	-1.3 ^f	1994-2006	-2.0 ^f	-2.0 ^g	-2.0 ^g
Prostate	1975-1987	0.9 ^f	1987-1991	3.0 ^f	1991-1994	-0.6	1994-2006	-4.1 ^f			-4.1 ^g	-4.1 ^g
Colon and rectum	1975-1984	-0.1	1984-1990	-1.4 ^f	1990-2002	-2.0 ^f	2002-2006	-3.9 ^f			-2.9 ^g	-3.9 ^g
Pancreas	1975-1986	-0.9 ^f	1986-2003	-0.2 ^f	2003-2006	1.0					0.2	0.7
Leukemia	1975-1995	-0.2 ^f	1995-2006	-0.8 ^f							-0.8 ^g	-0.8 ^g
Non-Hodgkin lymphoma	1975-1991	2.7 ^f	1991-1997	1.7 ^f	1997-2006	-3.0 ^f					-3.0 ^g	-3.0 ^g
Esophagus	1975-1985	0.7 ^f	1985-1994	1.2 ^f	1994-2006	0.4 ^f					0.4 ^g	0.4 ^g
Urinary bladder	1975-1983	-1.4 ^f	1983-1987	-2.7 ^f	1987-1993	0.1	1993-2003	-0.6 ^f	2003-2006	0.7	-0.2	0.4
Liver and intrahepatic bile duct	1975-1979	0.3	1979-1987	2.3 ^f	1987-1996	3.9 ^f	1996-1999	0.5	1999-2006	2.4 ^f	2.0 ^g	2.4 ^g
Kidney and renal pelvis	1975-1991	1.1 ^f	1991-2002	-0.1	2002-2006	-1.5 ^f					-0.7 ^g	-1.5 ^g
Stomach	1975-1994	-2.1 ^f	1994-2006	-3.7 ^f							-3.7 ^g	-3.7 ^g
Brain and other nervous system	1975-1977	4.4	1977-1982	-0.4	1982-1991	1.3 ^f	1991-2006	-1.0 ^f			-1.0 ^g	-1.0 ^g
Myeloma	1975-1994	1.5 ^f	1994-2006	-1.1 ^f							-1.1 ^g	-1.1 ^g
Oral cavity and pharynx	1975-1980	-0.9	1980-2006	-2.2 ^f							-2.2 ^g	-2.2 ^g
Melanoma of the skin	1975-1987	2.4 ^f	1987-1998	0.7 ^f	1998-2002	-1.5	2002-2006	2.0 ^f			0.3	2.0 ^g
Top 15 cancers for females^c												
Lung and bronchus	1975-1982	6.0 ^f	1982-1990	4.2 ^f	1990-1995	1.7 ^f	1995-2003	0.3 ^f	2003-2006	-0.9	-0.1	-0.6
Breast	1975-1990	0.4 ^f	1990-1995	-1.8 ^f	1995-1998	-3.3 ^f	1998-2006	-1.9 ^f			-2.0 ^g	-1.9 ^g
Colon and rectum	1975-1984	-1.0 ^f	1984-2001	-1.8 ^f	2001-2006	-3.4 ^f					-2.7 ^g	-3.4 ^g
Pancreas	1975-1984	0.8 ^f	1984-2006	0.1 ^f							0.1 ^g	0.1 ^g
Ovary	1975-1982	-1.2 ^f	1982-1992	0.3 ^f	1992-1998	-1.2 ^f	1998-2002	0.7	2002-2006	-1.4 ^f	-0.4	-1.4 ^g
Non-Hodgkin lymphoma	1975-1997	2.1 ^f	1997-2006	-3.7 ^f							-3.7 ^g	-3.7 ^g
Leukemia	1975-1980	0.7	1980-2000	-0.4 ^f	2000-2006	-1.6 ^f					-1.2 ^g	-1.6 ^g
Corpus and uterus, NOS	1975-1992	-1.5 ^f	1992-2006	0.0							0.0	0.0
Brain and other nervous system	1975-1992	1.0 ^f	1992-2006	-1.1 ^f							-1.1 ^g	-1.1 ^g
Liver and intrahepatic bile duct	1975-1978	-1.5	1978-1988	1.4 ^f	1988-1995	4.0 ^f	1995-2000	0.2	2000-2006	1.8 ^f	1.3 ^g	1.8 ^g
Myeloma	1975-1993	1.5 ^f	1993-2001	-0.4	2001-2006	-2.4 ^f					-1.5 ^g	-2.4 ^g
Stomach	1975-1987	-2.8 ^f	1987-1990	-0.3	1990-2006	-2.7 ^f					-2.7 ^g	-2.7 ^g
Kidney and renal pelvis	1975-1992	1.3 ^f	1992-2006	-0.6 ^f							-0.6 ^g	-0.6 ^g
Cervix uteri	1975-1982	-4.4 ^f	1982-1996	-1.6 ^f	1996-2003	-3.8 ^f	2003-2006	-0.7			-2.8 ^g	-1.5
Urinary bladder	1975-1986	-1.7 ^f	1986-2006	-0.4 ^f							-0.4 ^g	-0.4 ^g

AAPC indicates 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.

^bJoinpoint analyses with up to 4 joinpoints are based on rates per 100,000 persons and were age-adjusted to the 2000 U.S. standard population (19 age groups). Joinpoint (JP) Regression Program, version 3.2.0, January 2008, National Cancer Institute.

^cThe top 15 cancers were selected based on the sex-specific, age-adjusted death rates for 2001-2005 for all races combined and listed in rank order.

^dThe APC is based on rates that were age-adjusted to the 2000 U.S. standard population (19 age groups).

^eThe AAPC is a weighted average of the APCs calculated by Joinpoint.

^fThe APC is statistically significantly different from zero (2-sided $P < .05$).

^gThe AAPC is statistically significantly different from zero.

Cancer Incidence Rates 2002-2006 and Short-Term, Fixed-Interval Trends by Race/Ethnicity, 1997-2006

For all cancer sites combined, for both men and women by race/ethnicity, black men had the highest incidence rate during 2002-2006 (Table 3). For men in each population group, the highest incidence rates were observed for prostate cancer, followed by lung cancer and CRC, except among Hispanic men, whose rate for CRC was slightly higher than for lung cancer. Except for these 3 sites, the rank order of the top 15 cancers varied considerably among the racial/ethnic groups. Among women, non-Hispanic women and white women had the highest and second highest overall incidence rates, respectively, during 2002-2006. It should be noted that non-Hispanic and white are not mutually exclusive population categories. The most common cancer site for all women, regardless of race/ethnicity, was breast cancer. Lung cancer was the second most common cancer, and CRC ranked third for all races combined and for white, non-Hispanic, and AI/AN women. However, for black, API, and Hispanic women, CRC ranked second, and lung cancer ranked third. For all women, cancer of the uterus ranked fourth.

Among men, short-term trends in overall cancer incidence rates declined significantly during 1997-2006 for each racial/ethnic group, with the least decline observed for white and non-Hispanic men. Prostate cancer, the most frequently diagnosed cancer in men of all racial/ethnic groups, declined significantly for black men and Hispanic men. Lung cancer and CRC declined for men in each of the racial/ethnic population groups. Urinary bladder cancer declined for men in all races/ethnicities combined and for men who were white, black, non-Hispanic, and/or Hispanic. Cancer of the larynx declined for all groups of men except AI/AN men. However, kidney cancers increased among men in all of the racial/ethnic groups, and thyroid cancer increased among each racial/ethnic group that had adequate numbers of cases on which to calculate rates for estimating trends.

Women also experienced declining trends in overall cancer incidence among each race/ethnicity except AI/AN women. In contrast to men, the short-term AAPCs in

incidence rates for all cancers combined were similar among all races/ethnicities for women and changed less. Trends in incidence rates for breast cancer declined during 1997-2006 except among API women. Rates of CRC and invasive cancer of the cervix declined among all women except AI/AN women. Stomach cancer declined for all women. However, large increases in thyroid cancer were observed during this period for women in all racial/ethnic groups.

Cancer Death Rates 2002-2006 and Short-Term, Fixed Interval Trends by Race/Ethnicity, 1997-2006

Death rates for all cancers combined during 2002-2006 were highest for black men and women and lowest for API men and women (Table 4). Lung and prostate cancers and CRC were among the 3 leading causes of cancer death for men in each major racial/ethnic group except for API men, for whom liver cancer ranked second. Among most women, the leading causes of cancer death were lung and breast cancers, CRC, and pancreatic cancer. However, among Hispanic women, breast cancer was the leading cause of cancer death. Specific rankings for the other 15 types of cancer also varied within the racial/ethnic groups by sex.

During 1997-2006, short-term trends in death rates for all cancers combined decreased for all racial/ethnic groups and for both men and women, except for AI/AN women. Similarly, lung cancer mortality trends decreased for all racial/ethnic groups of men as did trends for prostate cancer and CRC except among AI/AN men. Liver cancer death rates increased for all men except API men, whose rates decreased, and except AI/AN men. Short-term trends for breast cancer death rates decreased in white, black, Hispanic, and non-Hispanic women; and CRC death rates decreased for all women except those who were Hispanic or AI/AN. Among women, short-term lung cancer death rate trends decreased for white, API, and Hispanic women but increased for AI/AN women. Short-term mortality trends for most other types of cancer had considerable variability among racial/ethnic population groups of women. Trends in death rates of pancreatic cancer increased for white men and women but decreased for black men and women.

Table 3. Incidence Rates for 2002-2006 and Fixed-Interval Trends for 1997-2006 for the Top 15 Cancers by Sex, Race, and Ethnicity, Selected Areas in the United States^{a,b}

Sex/Cancer Site or Type ^b	All Races/ Ethnicities			White ^c			Black ^c			API ^c			AI/AN (CHSDA Counties)			Hispanic ^c			Non-Hispanic ^c					
	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
Males																								
All sites ^f	556.5	-0.9 ^g	550.1	-0.9 ^g	626.0	-1.8 ^g	334.5	-1.6 ^g	441.2	-1.5 ^g	430.3	-1.3 ^g	567.7	-0.8 ^g										
Prostate	1	155.5	-0.9	1	231.9	-1.9 ^g	1	82.3	-1.3	1	108.8	-3.0	1	157.7	-0.8									
Lung and bronchus	2	86.4	-2.0 ^g	2	104.8	-2.7 ^g	2	50.6	-2.0 ^g	2	78.0	-3.2 ^g	3	89.4	-1.9 ^g									
Colon and rectum	3	59.0	-2.7 ^g	3	68.4	-2.1 ^g	3	44.1	-2.4 ^g	3	55.0	-2.9 ^g	2	59.8	-2.7 ^g									
Urinary bladder	4	37.9	-0.5 ^g	4	40.1	-0.5 ^g	6	15.4	0.2	4	21.1	-0.7 ^g	4	39.2	-0.4 ^g									
Non-Hodgkin lymphoma	5	23.1	0.1	6	23.7	0.2	7	14.5	-1.5 ^g	6	16.6	0.7	5	23.4	0.2									
Melanoma of the skin	6	22.6	2.7 ^g	5	24.9	2.7 ^g	26	1.1	-3.5	19	1.6	0.6	13	4.5	0.2									
Kidney and renal pelvis	7	19.6	2.5 ^g	7	19.7	2.6 ^g	4	20.6	2.7 ^g	4	24.5	2.3 ^g	6	18.2	2.1 ^g									
Leukemia	8	16.0	-0.6	8	16.4	-0.5	12	12.1	-1.1 ^g	11	11.9	-1.3	9	11.9	-1.0 ^g									
Oral cavity and pharynx	9	16.0	-1.1 ^g	9	15.9	-0.7 ^g	6	16.9	-3.2 ^g	8	13.1	-4.3 ^g	11	10.5	-3.0 ^g									
Pancreas	10	13.1	0.5 ^g	10	12.9	0.6 ^g	9	16.4	-0.2	9	9.5	-0.4	11	10.5	-0.2									
Stomach	11	10.0	-2.7 ^g	11	8.9	-2.6 ^g	8	16.7	-2.8 ^g	5	17.5	-3.1 ^g	7	14.7	0.3									
Liver and intrahepatic bile duct	12	9.1	3.4 ^g	14	8.0	3.4 ^g	11	12.5	4.0 ^g	4	21.4	-0.5	9	12.9	1.5									
Esophagus	13	8.6	0.2	12	8.6	0.2	14	10.4	-5.4 ^g	13	4.0	-2.0	12	6.9	-5.0									
Brain and other nervous system	14	7.9	-0.5 ^g	13	8.4	-0.4 ^g	15	4.7	-0.8	14	3.9	-2.1 ^g	16	5.0	1.1									
Larynx	15	7.1	-3.0 ^g	15	6.9	-2.8 ^g	13	11.2	-3.0 ^g	17	2.6	-5.5 ^g	14	6.2	-2.1									
Myeloma	16	7.0	-0.3	16	6.5	-0.1	10	13.3	-0.3	15	3.8	-2.3	15	6.0	-5.6 ^g									
Thyroid	18	4.9	5.8 ^g	18	5.1	5.9 ^g	19	2.6	4.7 ^g	12	4.3	4.3 ^g	18	3.0	h									
Females																								
All sites ^f	414.8	-0.5 ^g	420.0	-0.5 ^g	389.5	-0.4 ^g	276.3	-0.5 ^g	369.3	-0.3	326.8	-0.6 ^g	422.9	-0.4 ^g										
Breast	1	121.8	-1.5 ^g	1	123.5	-1.6 ^g	1	81.6	-0.3	1	91.7	-1.5 ^g	1	124.7	-1.4 ^g									
Lung and bronchus	2	55.5	0.1	2	57.1	0.2 ^g	3	27.6	-0.7	2	56.1	1.0	3	57.9	0.3 ^g									
Colon and rectum	3	43.6	-2.0 ^g	3	42.6	-2.2 ^g	2	33.1	-1.4 ^g	3	44.7	-1.8	2	44.2	-2.0 ^g									
Corpus and uterus, NOS	4	23.6	-0.1	4	24.1	-0.3	4	15.4	1.4 ^g	4	19.5	0.4	4	24.0	-0.2									
Non-Hodgkin lymphoma	5	16.3	-0.2	5	16.8	-0.1	6	10.4	-1.2	6	14.7	-0.1	5	16.4	-0.1									
Melanoma of the skin	6	14.6	3.2 ^g	6	16.5	3.3 ^g	28	1.0	-0.2	21	1.3	0.7	17	4.3	0.8									
Thyroid	7	14.2	7.4 ^g	7	14.8	7.4 ^g	11	8.7	6.9 ^g	5	9.6	3.8 ^g	6	15.9	3.6 ^g									
Ovary ⁱ	8	13.0	-1.7 ^g	8	13.5	-1.7 ^g	9	9.9	-2.4	8	9.3	-1.7 ^g	7	14.3	7.5 ^g									
Kidney and renal pelvis	9	10.2	3.1 ^g	9	10.3	3.2 ^g	8	10.6	2.8 ^g	14	4.5	2.9 ^g	8	13.2	-1.7 ^g									
Pancreas	10	10.2	0.7 ^g	11	9.9	0.8 ^g	5	13.5	0.0	10	7.8	-0.1	8	10.2	3.1 ^g									
Leukemia	11	9.6	-0.4	12	9.9	-0.4	13	7.5	-1.1	12	5.7	-1.2 ^g	11	9.6	-0.3									

(Continued)

Table 3. (Continued)

Sex/Cancer Site or Type ^b	All Races/ Ethnicities		White ^c		Black ^c		API ^e		AI/AN (CHSDA Counties)		Hispanic ^e		Non-Hispanic ^e	
	Rank	Rate ^d	Rank	Rate ^d	Rank	Rate ^d	Rank	Rate ^d	Rank	Rate ^d	Rank	Rate ^d	Rank	Rate ^d
Urinary bladder	12	9.6	10	10.1	14	6.9	15	3.8	16	5.1	14	5.5	11	9.9
Cervix uteri	13	8.3	13	7.9	7	11.1	11	7.6	10	9.4	7	12.7	13	7.8
Oral cavity and pharynx	14	6.1	14	6.1	15	5.5	13	5.2	14	5.6	18	3.9	14	6.3
Brain and other nervous system	15	5.7	15	6.1	17	3.6	16	3.1	19	3.7	16	4.8	15	5.8
Stomach	16	4.9	16	4.2	12	8.5	7	9.8	12	7.3	11	8.6	17	4.6
Myeloma	17	4.6	17	4.1	10	9.6	17	2.7	15	5.2	15	4.8	16	4.6
Liver and intrahepatic bile duct	18	3.1	18	2.8	16	3.8	9	8.1	13	6.8	13	6.2	18	2.9

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

^aSource: Surveillance, Epidemiology, and End Results and National Program of Cancer Registries areas reported by the North American Association of Central Cancer Registries as meeting high-quality data standards for the specified time periods.

^bCancers are sorted in descending order according to sex-specific rates for all races/ethnicities. More than 15 cancers may appear under males and females to include the top 15 cancers in every race/ethnicity group.

^cWhite, black, API, and AI/AN include Hispanic and non-Hispanic; the race and ethnicity categories are not mutually exclusive.

^dRates are per 100,000 persons and were age-adjusted to the 2000 U.S. standard population (19 age groups).

^eThe annual percent change (APC) is based on rates that were age-adjusted to the 2000 U.S. standard population (19 age groups).

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

^gThe APC is statistically significantly different from zero (2-sided $P < .05$).

^hThis statistic could not be calculated. The APC is based on fewer than 10 cases for at least 1 year within the time interval.

2002-2006 Rates for all races/ethnicities, white, black, AI/AN, API, Hispanic, and non-Hispanic (43 states): Alabama, Alaska, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Texas, Utah, Virginia, Washington, West Virginia, Wyoming.

1997-2006 APCs for all races/ethnicities, white, black, AI/AN, API, Hispanic, and non-Hispanic (33 states): Alaska, California, Colorado, Connecticut, Delaware, Florida, Metropolitan Atlanta, Hawaii, Idaho, Illinois, Iowa, Kentucky, Louisiana, Maine, Massachusetts, Michigan, Minnesota, Montana, Nebraska, Nevada, New Jersey, New Mexico, New York, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Texas, Utah, Washington, West Virginia, Wyoming.

Table 4. Death Rates for 2002-2006 and Fixed-Interval Trends for 1997-2006 for the Top 15 Cancers by Sex, Race, and Ethnicity in the United States^{a,b}

Sex/Cancer Site or Type ^b	All Races/ Ethnicities							White ^c	Black ^c	API ^c	AI/AN ^c	AI/AN (CHSDA Counties)	Hispanic ^{c,d}	Non-Hispanic ^{c,d}				
	Rank Rate ^e	AAPC ^f	Rank Rate ^e	AAPC ^f	Rank Rate ^e	AAPC ^f	Rank Rate ^e								AAPC ^f	Rank Rate ^e	AAPC ^f	Rank Rate ^e
Males																		
All sites	229.9	-1.7 ^g	226.7	-1.5 ^g	304.2	-2.5 ^g	135.4	-2.1 ^g	146.4	-2.8 ^g	183.3	-1.2 ^g	154.8	-2.2 ^g	235.0	-1.6 ^g		
Lung and bronchus	1	70.5	-2.0 ^g	1	69.9	-1.8 ^g	1	36.9	41.2	-4.2 ^g	1	48.0	33.9	33.9	-3.0 ^g	1	73.3	-1.8 ^g
Prostate	2	25.6	-4.0 ^g	2	23.6	-3.9 ^g	4	10.6	16.8	-3.9 ^g	3	20.0	19.6	19.6	-3.5 ^g	2	25.9	-4.0 ^g
Colon and rectum	3	21.9	-2.8 ^g	3	21.4	-3.0 ^g	3	13.8	15.3	-3.3 ^g	2	20.0	16.1	16.1	-1.8 ^g	3	22.4	-2.7 ^g
Pancreas	4	12.3	0.1	4	12.2	0.3 ^g	4	8.1	7.1	0.6	6	9.1	9.1	9.1	-0.1	4	12.5	0.2 ^g
Leukemia	5	9.8	-0.8 ^g	5	10.1	-0.7 ^g	8	5.0	4.5	-0.8	9	5.9	6.2	6.2	-1.6 ^g	5	10.0	-0.7 ^g
Non-Hodgkin lymphoma	6	9.0	-3.0 ^g	6	9.3	-2.9 ^g	11	5.4	4.0	-5.1 ^g	10	5.2	6.4	6.4	-3.9 ^g	6	9.1	-2.8 ^g
Esophagus	7	7.8	0.4 ^g	8	7.9	1.2 ^g	7	3.1	5.1	1.2	8	6.7	4.1	4.1	-2.1 ^g	7	8.0	0.6 ^g
Urinary bladder	8	7.5	-0.2	7	7.9	0.0	13	2.7	2.6	^h	14	2.7	3.9	3.9	-0.8	8	7.7	0.0
Liver and intrahepatic bile duct	9	7.5	2.1 ^g	9	6.8	2.2 ^g	6	15.0	7.9	-0.2	4	10.3	11.3	11.3	1.3 ^g	9	7.2	2.1 ^g
Kidney and renal pelvis	10	6.0	-0.6 ^g	10	6.1	-0.5 ^g	12	2.4	6.6	-1.2	7	9.0	5.2	5.2	0.0	10	6.0	-0.6 ^g
Stomach	11	5.5	-3.7 ^g	12	4.8	-3.8 ^g	5	9.6	6.4	-1.2	5	9.8	8.3	8.3	-3.3 ^g	12	5.3	-3.8 ^g
Brain and other nervous system	12	5.3	-1.1 ^g	11	5.7	-1.1 ^g	15	2.5	2.3	-2.9 ^g	13	2.9	3.3	3.3	-1.8 ^g	11	5.5	-1.0 ^g
Myeloma	13	4.5	-1.1 ^g	14	4.3	-1.0 ^g	9	1.9	3.3	-1.4	11	4.3	4.3	4.3	-1.9	13	4.6	-1.1 ^g
Oral cavity and pharynx	14	3.9	-1.8 ^g	15	3.7	-1.5 ^g	10	3.2	3.0	-3.8	12	3.6	2.5	2.5	-3.8 ^g	15	4.1	-1.6 ^g
Melanoma of the skin	15	3.9	0.2	13	4.4	0.3	22	0.5	1.1	^h	16	1.6	0.9	0.9	-3.1 ^g	14	4.2	0.5
Larynx	16	2.3	-2.2 ^g	16	2.1	-1.9 ^g	14	0.7	1.5	-7.0 ^g	15	1.9	1.9	1.9	-4.2 ^g	16	2.3	-2.0 ^g
Soft tissue including heart	17	1.4	-1.5 ^g	18	1.4	-1.2 ^g	16	0.9	0.8	^h	19	1.0	1.0	1.0	-3.2 ^g	18	1.5	-1.3 ^g
Females																		
All sites	157.8	-1.0 ^g	157.3	-0.9 ^g	183.7	-1.4 ^g	95.1	-1.1 ^g	110.1	-0.7 ^g	140.1	0.2	103.9	-1.1 ^g	161.6	-0.9 ^g		
Lung and bronchus	1	40.9	-0.1	1	41.9	-0.1 ^g	1	18.2	28.3	1.1	1	33.5	14.4	14.4	-0.8 ^g	1	42.8	0.1
Breast	2	24.5	-1.9 ^g	2	23.9	-2.0 ^g	2	12.5	14.3	0.2	2	17.6	15.5	15.5	-2.1 ^g	2	25.2	-1.8 ^g
Colon and rectum	3	15.4	-2.6 ^g	3	14.9	-2.6 ^g	3	10.0	10.2	-3.4 ^g	3	13.7	10.7	10.7	-0.6	3	15.7	-2.6 ^g
Pancreas	4	9.3	0.5	4	9.1	0.5 ^g	4	7.0	6.6	2.0	4	7.8	7.5	7.5	0.8 ^g	4	9.4	0.6 ^g
Ovary	5	8.8	-0.5 ^g	5	9.1	-0.3	5	4.9	5.4	2.2	5	6.8	6.0	6.0	0.8	5	9.0	-0.4 ^g
Non-Hodgkin lymphoma	6	5.7	-3.3 ^g	6	5.9	-3.3 ^g	11	3.7	3.3	-3.1	8	4.4	4.6	4.6	-3.3 ^g	6	5.8	-3.4 ^g
Leukemia	7	5.5	-1.0 ^g	7	5.7	-0.7	9	2.9	3.1	-0.8	10	3.6	4.0	4.0	-1.2	7	5.6	-1.0 ^g

(Continued)

Table 4. (Continued)

Sex/Cancer Site or Type ^b	Rank Rate ^a	APC ^c	Rank Rate ^a	White ^e	Black ^e	API ^e	AI/AN ^e	AI/AN (CHSDA Counties)	Hispanic ^{c,d}	Non-Hispanic ^{c,d}														
Corpus and uterus, NOS	8	4.1	0.3 ^g	8	3.9	0.2	6	7.2	0.7 ^g	10	2.5	2.0 ^g	13	2.2	-0.8	13	3.0	^h	10	3.1	0.1	8	4.2	0.4 ^g
Brain and other nervous system	9	3.5	-1.4 ^g	9	3.8	-1.2 ^g	16	2.1	-2.4 ^g	12	1.6	0.7	16	1.3	^h	17	1.3	^h	14	2.4	0.0	9	3.6	-1.3 ^g
Liver and intrahepatic bile duct	10	3.2	1.2 ^g	10	2.9	1.2 ^g	12	3.9	0.4	5	6.6	-0.3	6	4.6	1.1	6	6.5	1.6	6	5.1	1.1	10	3.0	1.1 ^g
Myeloma	11	3.0	-1.3 ^g	12	2.7	-1.2 ^g	7	5.8	-2.3 ^g	13	1.5	-1.3	11	2.5	-0.4	12	3.3	0.0	12	2.6	-1.1	11	3.0	-1.3 ^g
Stomach	12	2.8	-2.8 ^g	13	2.4	-2.9 ^g	8	5.3	-3.5 ^g	6	5.8	-3.7 ^g	8	3.2	-7.3 ^g	7	4.6	-6.9 ^g	7	4.8	-2.1	13	2.7	-3.1 ^g
Kidney and renal pelvis	13	2.7	-0.6 ^g	11	2.8	-0.5 ^g	14	2.7	-0.6	15	1.2	-1.1	10	2.9	-1.6	9	4.2	0.8	13	2.4	0.0	12	2.7	-0.5 ^g
Cervix uteri	14	2.5	-2.7 ^g	15	2.2	-2.4 ^g	10	4.6	-4.2 ^g	11	2.2	-4.8 ^g	12	2.5	-7.2	11	3.4	-3.7	11	3.1	-2.4	14	2.4	-3.0 ^g
Urinary bladder	15	2.2	-0.8 ^g	14	2.2	-0.7 ^g	13	2.8	-1.3 ^g	16	1.0	-1.0	18	1.2	^h	18	1.1	^h	15	1.3	-0.3	15	2.3	-0.7 ^g
Esophagus	17	1.7	-0.9 ^g	17	1.6	-0.2	15	2.7	-4.2 ^g	17	0.9	-2.8	15	1.4	^h	15	1.7	^h	17	0.9	-2.6	17	1.8	-0.7 ^g
Oral cavity and pharynx	18	1.5	-2.4 ^g	18	1.4	-2.2 ^g	17	1.6	-4.7 ^g	14	1.3	-0.1	17	1.2	^h	16	1.5	^h	19	0.8	-2.1	18	1.5	-2.3 ^g
Gallbladder	20	0.8	-1.8 ^g	20	0.8	-1.8 ^g	19	1.0	-0.6	18	0.8	-3.8 ^g	14	1.5	-3.3	14	2.4	^h	16	1.3	-1.7	20	0.8	-1.9 ^g

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

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

^bCancers are sorted in descending order according to sex-specific rates for all races/ethnicities. More than 15 cancers may appear under males and females to include the top 15 cancers in every race/ethnicity group.

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

^dData for Hispanic and non-Hispanic exclude the District of Columbia, Maine, Minnesota, New Hampshire, and North Dakota.

^eRates are per 100,000 persons and were age-adjusted to the 2000 U.S. standard population (19 age groups).

^fThe AAPC is a weighted average of the annual percent changes (APCs) calculated by Joinpoint over the time period 1997-2006. Joinpoint analyses with up to 2 joinpoints are based on rates per 100,000 persons and were age-adjusted to the 2000 U.S. standard population (19 age groups). Joinpoint (JP) Regression Program, version 3.3.1, April 2008, National Cancer Institute.

^gThe AAPC is statistically significantly different from zero.

^hThis statistic could not be calculated. The average APC is based on fewer than 10 cases for at least 1 year within the time interval.

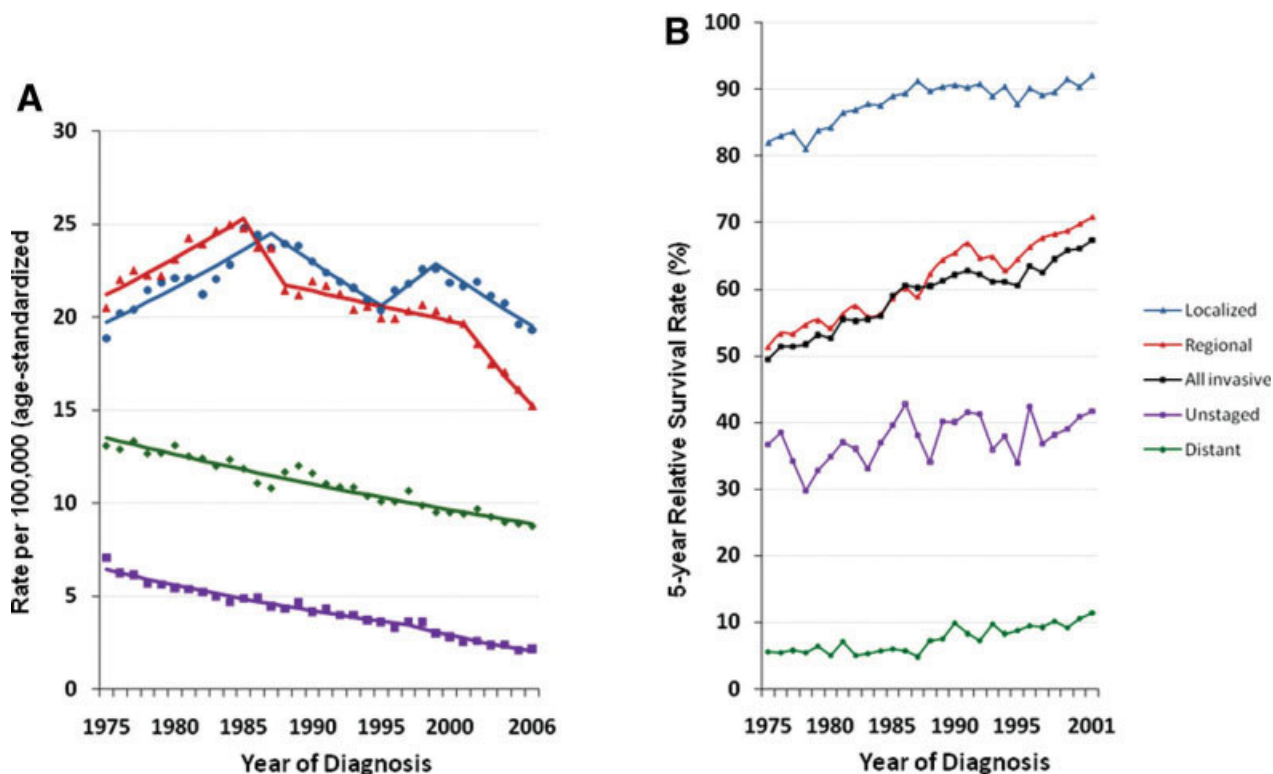


Figure 2. (A) Trends in stage-specific age-standardized colorectal cancer (CRC) incidence rates by year of diagnosis (1975–2006) for all races, both sexes. Joinpoint regression with up to 4 joinpoints are calculated using Version 3.3.1 (April 2008) from the National Cancer Institute. (B) Trends in CRC 5-year relative survival by stage at diagnosis and year of diagnosis (1975–2001) for all races, both sexes. Data are from the Surveillance, Epidemiology, and End Results (SEER) 9 areas which cover about 10% of the U.S. population. Stage analyses were based on Extent of Disease (EOD) and Collaborative Stage (CS) Data Collection System. Incidence rates are age-adjusted to the 2000 US Std Population (19 age groups). Relative survival was calculated with the SEER*Stat software (<http://www.seer.cancer.gov/seerstat>) version 6.5.2: NCI; 2009.

CRC Incidence (by Age, Subsite, and Stage), Mortality, and Stage-Specific Survival Trends

Long-term incidence trends for CRC (based on SEER 9) have been fairly consistent in men and women (Table 1), with increasing incidence (for men) during 1975–1985, marked declines during 1985–1995 for men and women followed by a short nonsignificant increase (1995–1998), and marked declines during 1998–2006. CRC death rates (Table 2) have declined since 1984 in both men and women, with an accelerated rate of decline since 2002 (for men) and 2001 (for women). During the most recent decade (1997–2006, based on pooled data) (see Table 3), short-term trends in CRC incidence declined for all racial/ethnic groups, for men, and for women (except AI/

ANs); the fastest annual rate of decline occurred among men and women aged ≥ 65 years (a data table is available at www.seer.gov/report_to_nation/1975_2006 [Supporting Information Table 2]) compared with younger individuals. In contrast, short-term incidence trends increased annually for individuals aged < 50 years within most population groups with few exceptions. Incidence rates by major anatomic subsites (proximal colon, distal colon, rectum) varied considerably by race, sex, and age (see the data table at www.seer.cancer.gov/report_to_nation/1975_2006 [Supporting Information Table 2]). Incidence rates for all ages combined for distal colon and rectal cancers decreased among men and women in every racial/ethnic group except for distal colon cancer among AI/AN men and women. In contrast, among individuals

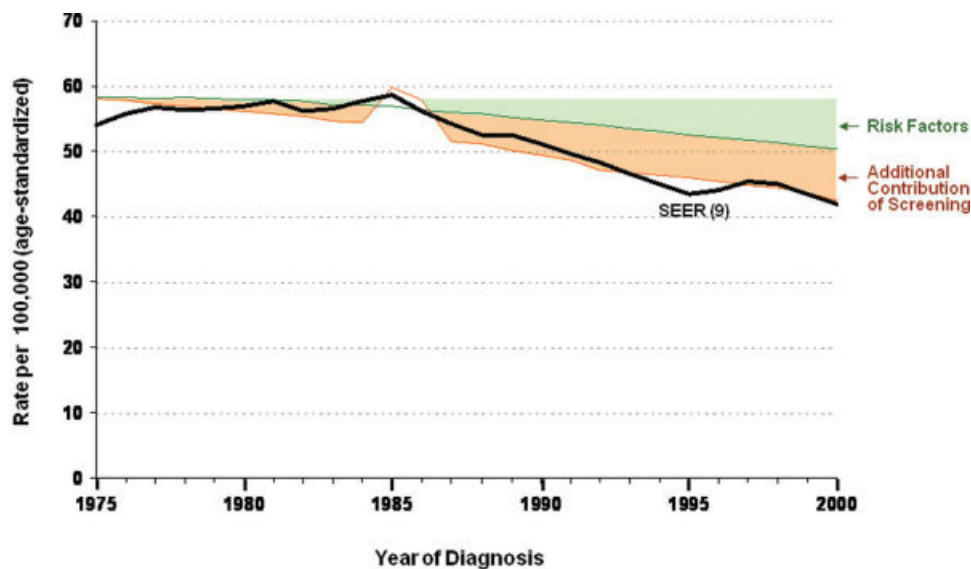


Figure 3. Partition of past trends in colorectal cancer incidence (1975–2000). The age-adjusted rates are given by year of colorectal cancer (CRC) diagnoses. The black line is the observed Surveillance, Epidemiology, and End Results (SEER) CRC incidence rates based on first primary CRC. The red line is the microsimulation screening analysis (MISCAN) model estimate of the CRC incidence rate in the time period 1975–2000 based on the natural history of the CRC overlaid by the changes in the prevalence of risk factors and the uptake of CRC screening during this time period. The green line is the MISCAN model estimate of CRC incidence in this time period if only risk factor changes had occurred without screening increases. The shaded green area represents the impact of risk factor changes on incidence in the time period 1965–2000 (see text). The orange area represents the additional impact of increases in screening over and above the changes due to risk factors alone for this period. Rates are based on the first primary CRC and include the primary sites of C18.0 C18.2-C18.9, C19.9, C20.9 and the ICD-03 histologies of: 8000–8001, 8010, 8020, 8140, 8210–8211, 8220–8221, 8260–8263, 8480–8481, 8490. Rates do not include cases that are from a reporting source of death certificate only or autopsy only.

aged <50 years, incidence rates for distal colon and rectal cancers increased in men and women of all race/ethnicities combined, in white men and women, and in black men. Rates for proximal colon cancer decreased in men and women of all race/ethnicities combined but decreased by subgroup only for white men and women, API men, and Hispanic women.

Trends in stage-specific incidence rates ([Fig. 2A] and a data table [available at www.seer.cancer.gov/report_to_nation/1975-2006] [Supporting Information Table 3]) for the SEER 9 data revealed annual increases in the incidence of localized cancer from 1975 to 1987 (APC = 1.8%), declines from 1987 to 1995 (APC = -2.1%), and nonsignificant increases from 1995 to 1999, followed by decreases between 1999 and 2006 (APC = -2.2%). Incidence rates of regional cancer increased between 1975 and 1985 (APC = 1.8%), decreased markedly but not significantly from 1985 to 1988 (APC = -5.0%), and decreased significantly thereafter by 0.8% per year from 1988 to 2001 and by 5.0% per year between 2001 and

2006. Incidence rates of distant cancer decreased steadily between 1975 and 2006 by 1.3% per year. Incidence rates of unstaged cancer decreased by 2.8% per year between 1975 and 1997 and by 5.7% per year during the 10-year interval from 1997 to 2006. CRC 5-year relative survival has improved throughout the period 1975–2001 (Fig. 2B) for all patients in each stage category. Relative survival rate at 5 years for the most recent diagnosis years are 90% for localized disease, 70% for regional disease, and 12% for distant disease.

Past and Future Trends in CRC Incidence and Death Rates: Impact of Risk Factors, Screening, and Treatment

Figure 3 illustrates the age-standardized CRC incidence rates by calendar year 1975–2000 for SEER 9 registries (adjusted to represent first primary CRCs) and for the MISCAN-Colon model estimated rates. There are 2 lines with estimated rates for MISCAN. One line represents

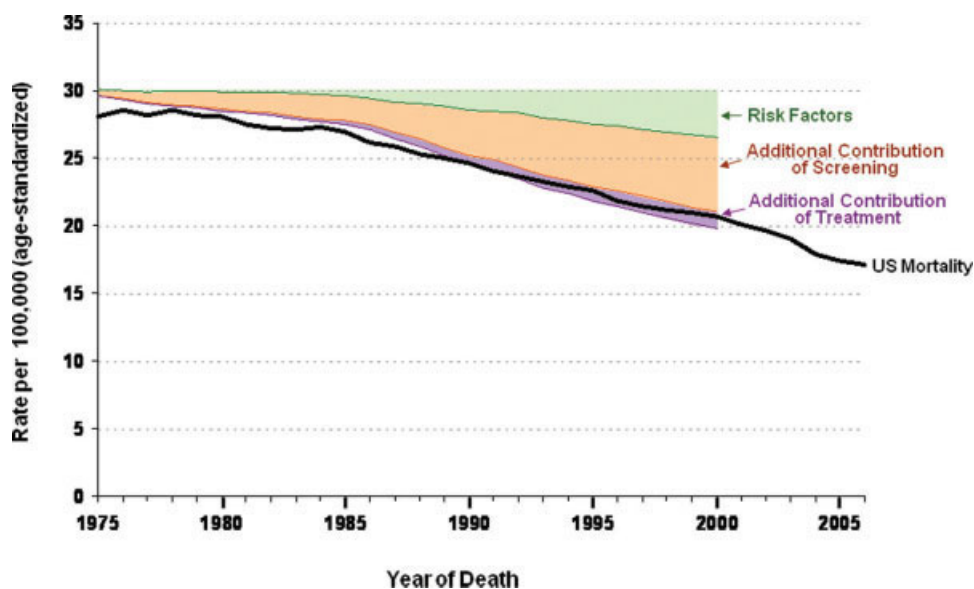


Figure 4. Partition of past trends in colorectal cancer mortality (1975–2000). The age-adjusted rates are given by year of colorectal cancer (CRC) diagnoses. The black line is the observed US CRC age-adjusted death rate for 1975–2005. The purple line is the microsimulation screening analysis (MISCAN) model estimate of CRC in the time period 1975–2000 based on the natural history of CRC overlaid by the changes in the prevalence of risk factors, the uptake of CRC screening, and dissemination of treatment during this time period. The red line is the MISCAN model estimate of CRC in the time period 1975–2000 based on the natural history of CRC overlaid by the changes in the prevalence of risk factors and the uptake of CRC screening during this time period minus treatment. The green line is the MISCAN model estimate of CRC mortality in this time period if only risk factor changes had occurred and not increases in screening and treatment as well. The shaded green area represents the impact of risk factor changes on mortality in the time period 1965–2000 (see text). The orange area represents the additional contribution to the decline in mortality of screening increases over and above that due to changes in risk factors in this period. The purple area represents the additional contribution of treatment over and above that of risk factor and screening effects on the mortality decline. Source: CDC National Center for Health Statistics, National Vital Statistics System. Heron M, Hoyert DL, Murphy SL, Xu J, Kochanek KD, Tejada-Vera B. Deaths: Final data for 2006. National Vital Statistics Reports, April 17, 2009, 57(14).

the model-predicted CRC incidence rates based on observed trends in risk factor prevalence and screening uptake. The other line represents the model-predicted rates when only changes in risk factors would have occurred and no screening had taken place. The overall observed decline in CRC incidence was 22% for 1975–2000. The MISCAN model-predicted decline without screening was 11%, indicating that changes in risk factors accounted for 50% of the overall decline in incidence rates during 1975–2000. Screening affected the CRC incidence rates adversely in the short term but then accounted for 50% of the CRC incidence decline for the period.

Figure 4 illustrates the age-standardized observed and MISCAN model-predicted CRC US death rates by calendar year from 1975–2000. There are 3 lines with estimated death rates. One line represents the model-predicted CRC mortality based on observed trends in risk factor prevalence, screening uptake, and treatment use. Another

line represents the model-predicted death rates when only risk factors and screening changed over time, and the last line represents the model-predicted mortality for changes in risk factors only. The overall observed decline in CRC mortality was 26% for 1975–2000. The model predicted that, with only changes in risk factors, CRC mortality would decrease by 9%, explaining 35% of the observed mortality decline. Screening decreased mortality by another 14%, explaining 53% of the mortality reduction, whereas treatment added another 3% decline, explaining the final 12% of the observed decline in CRC mortality.

The microsimulation modeling also projected future CRC mortality based on differing intensities of cancer control, including no change (pre-2000, frozen), continued trends, and optimistic trends in the prevalence of interventions (Fig. 5).²⁹ Without changes in risk factors, screening, and treatment (frozen as of 2000), the decline in CRC mortality may only be 17%. However, the

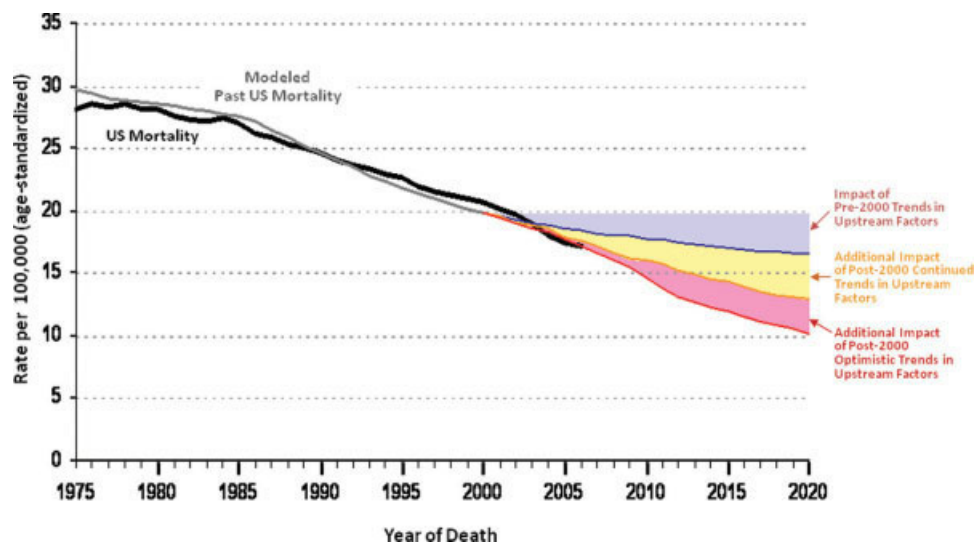


Figure 5. Projections of colorectal cancer mortality with differing intensities of cancer control interventions (2000–2020). The age-adjusted colorectal cancer (CRC) death rates are presented by year of death. The black line is the age-adjusted US mortality rate (1975–2006). The gray line is the microsimulation screening analysis (MISCAN) modeling of the age-adjusted mortality 1975 to 2000 based on the past trends in risk factors, screening, and treatment (the purple line of Figure 3). There are 3 levels of cancer control interventions of risk factors, screening, and treatment. The blue line represents the projected CRC mortality if the upstream factors for risk factors, screening, and treatment remain at the same level as for 2000. This scenario is called frozen (at 2000). The orange line represents the projected CRC mortality if the upstream factors continued according to the trend of these factors in 1995–2000. This scenario is called continuing trends. The red line represents the projected CRC mortality if the upstream factors for risk factors, screening, and treatment improve over and above that of continued trends to an optimistic level for each factor. This scenario is called optimistic trends. The blue area represents the improvement in CRC mortality based on the pre-2000 trends in upstream factors. The yellow area represents the additional impact of post-2000 continued trends in upstream factors. The red area represents the additional impact of post-2000 optimistic trends in upstream factors. Source: CDC National Center for Health Statistics, National Vital Statistics System. Heron M, Hoyert DL, Murphy SL, Xu J, Kochanek KD, Tejada-Vera B. Deaths: Final data for 2006. National Vital Statistics Reports, April 17, 2009, 57(14).

MISCAN-Colon model predicts a 36% overall decline in CRC mortality from 2000 to 2020 if current trends in risk factors, screening, and treatment continue. If we can accelerate the projected trends, then an overall mortality reduction of 50% by 2020 is possible. Figure 6 illustrates the contribution of the 3 types of interventions to this optimistic reduction in mortality. Risk factor modifications, although they require the longest time to produce an impact, will have a sizable effect by 2020. Increases in the proportion of adults screened and in the use of endoscopic CRC screening will provide the largest reduction in future death rates with application of current state-of-screening technologies, risk factor modification, and use of current treatment practices.

DISCUSSION

This Annual Report to the Nation documents continued declines in incidence and mortality rates from all cancers combined among both men and women. However, cancer

incidence and mortality vary by specific types of cancer and by sex and racial/ethnic group. Decreases in incidence and death rates are greater for men than for women (Tables 1 and 2), but overall rates continue to be much higher for men than for women (Tables 3 and 4). Incidence rates for the 3 leading causes of cancer for men (prostate and lung cancer and CRC) all declined along with 3 more of the top 15 cancers (ie, oral cavity, stomach, and brain) (Table 1), as in past years. However, incidence rates increased for kidney, liver, and esophageal cancers and for leukemia, myeloma, and melanoma; rates did not change for bladder or pancreatic cancers or for NHL. For the top 3 cancers among women, breast cancer and CRC incidence rates declined, but lung cancer incidence rates increased. Of the remaining 15 leading cancers for women, incidence rates also declined for cancers of the uterus, ovary, cervix, and oral cavity but increased for cancers of the lung, thyroid, pancreas, bladder, and kidney and for NHL, melanoma, and leukemia.

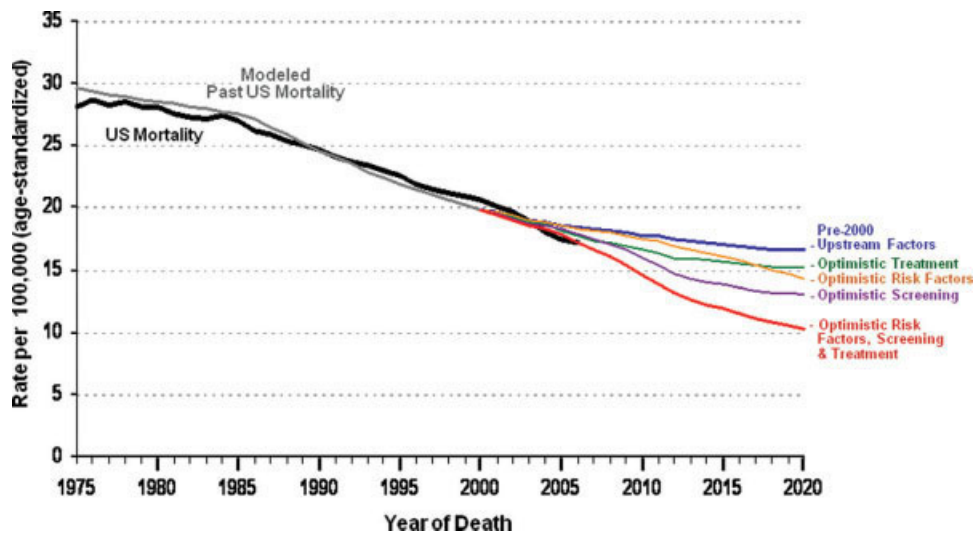


Figure 6. Contributions of risk factors, screening, and treatment to optimistic projections of colorectal cancer (CRC) mortality (2000–2020). The black line is the age-adjusted US death rate (1975–2006) by age at death. The gray line is the microsimulation screening analysis (MISCAN) modeling of the age-adjusted mortality 1975 to 2000 based on the past trends in risk factors, screening, and treatment (the purple line of Figure 3). The heavy blue line is the MISCAN model projection based on pre-2000 upstream factors (frozen scenario) (blue line of Figure 5). The next lines represent the individual components of the opportunistic trends models. The green line represents the projected age-adjusted CRC mortality if only optimistic treatment interventions are implemented. The orange line represents the age-adjusted CRC death rate if only optimistic risk factor interventions were implemented. The purple line represents the CRC mortality rate if only optimistic screening was implemented. The heavy red line represents the CRC death rate for the combined effect of implementing risk factor, screening, and treatment interventions (same line as red line in Figure 5). Source: CDC National Center for Health Statistics, National Vital Statistics System. Heron M, Hoyert DL, Murphy SL, Xu J, Kochanek KD, Tejada-Vera B. Deaths: Final data for 2006. National Vital Statistics Reports, April 17, 2009, 57(14).

The continued decline in death rates (Table 2) from all cancers combined for men and women reflects the impact of increased screening, reduction of risk factors, and improved treatment. Risk factors generally affect disease development over the long term rather than the short term, so education and prevention efforts begun decades ago may be reflected in the current decreased cancer mortality. Decreases in cancer mortality rates for men were greater than for women; but, as with incidence rates, cancer mortality rates generally are much higher for men than for women. Of the 15 most frequently occurring cancers among men in the most recent time period (Table 2), decreases occurred in death rates for cancers of the stomach, kidney, brain, lung, prostate, and oral cavity and for CRC, leukemia, NHL, and myeloma. Death rates among men increased for melanoma and for liver and esophageal cancers. Among women in the most recent time period (Table 2), mortality rates decreased for CRC and for cancers of the stomach, kidney, brain, breast, ovary, and bladder as well as for leukemia, NHL, and myeloma; however,

death rates for women increased for pancreatic and liver cancers. Liver cancer was the only cancer for which death rates increased for both men and women, suggesting a need to identify and implement interventions that can reduce mortality from this cancer.

Of the leading cancers, prostate cancer is of special note, because it is the most frequently diagnosed cancer and is second leading cause of cancer death among men. Incidence for prostate cancer has fluctuated through the years, increasing during 1975–1992, decreasing during 1992–1995, increasing (nonsignificantly) during 1995–2000, and decreasing again during 2000–2006 (Table 1). The few randomized trials on prostate cancer screening produced conflicting results with various methodologies.^{56,57} Consequently, comparative microsimulation modeling is being used to better understand the progression of the disease, the impact of screening on mortality, and cost implications of expanded prostate screening.^{58–60} A CISNET prostate cancer project is using available data to model the impact of screening on prostate cancer incidence and mortality. Screening for breast cancer, the most

frequently diagnosed cancer and the second leading cause of cancer death among women, already is recommended for women.⁶¹ Breast cancer incidence also has fluctuated with increases and decreases over time (Table 1) but declined 1.5% per year during 2002-2006 (Table 3).

Among racial and ethnic groups, the highest cancer death rates occurred among black men and women, and the lowest rates occurred among API men and women (Table 4). However, pancreatic cancer death rates, the fourth most common cause of cancer death in the United States, increased among white individuals but decreased among black individuals. The 3 leading causes of cancer deaths by racial and ethnic group for men were lung and prostate cancers and CRC. This ranking varied only for API men, for whom lung and liver cancers and CRC were the leading cancers. Among women by racial/ethnic group, the leading causes of cancer deaths were lung and breast cancers and CRC, except for Hispanic women, for whom breast cancer ranked first. Mortality for the top 3 cancers declined for men among all racial and ethnic groups, and breast and CRC declined for women. CRC death rates decreased for women in all racial and ethnic groups except AI/AN and Hispanic women. The differences and fluctuations in death rates for specific cancers for different racial and ethnic groups and for men and women suggest differences in risk behaviors, socioeconomic status, and access to and use of screening and treatment.⁶²⁻⁶⁴

This report highlights CRC, currently the third most frequently diagnosed cancer and the second leading cause of cancer deaths in the United States for men and women combined. Globally, CRC incidence in economically transitioning countries continues to rise because of increased exposure to risk factors; however, in economically developed countries, rates have stabilized or are declining.^{65,66} In the United States, an estimated 147,000 individuals will be diagnosed with CRC in 2009, and approximately 50,000 will die of the disease.^{62,67}

Table 1 shows that, since 1985, CRC incidence rates have declined for both men and women except during 1995-1998. The age-adjusted CRC incidence rates for 1997-2006 declined among both men and women aged ≥ 50 years but increased among those aged < 50 years (a data table is available at www.seer.cancer.gov/report_to_nation/1975_2006 [Supporting Information Table 2]). Although men generally had slightly greater rates of

decline than women, incidence rates for men remained considerably higher than for women. Although $> 90\%$ of newly diagnosed cases of CRC occurred among individuals aged ≥ 50 years (a data table is available at www.seer.cancer.gov/report_to_nation/1975_2006 [Supporting Information Table 2]), increasing incidence among younger men and women is of concern, suggesting future increases in CRC as these populations age that could be exacerbated by increasing prevalence of obesity and unfavorable dietary changes.⁶⁸ Individuals aged < 50 years also are more likely to be diagnosed with later stage and less differentiated CRC⁶⁹ than older individuals, likely reflecting the benefits of screening in older populations. Age-adjusted incidence rates for individuals aged < 50 years were highest among black individuals and lowest for individuals of Hispanic ethnicity but are increasing most rapidly for the AI/AN population. For older adults, incidence rates were highest among black individuals and were disproportionately high among those ages 50-64 years. Individuals aged ≥ 65 years are more at risk for CRC, have higher incidence (with rapid annual declines in trends), and have higher rates of CRC test use compared with individuals aged < 65 years.^{70,71} The burden of CRC mortality is concentrated in older individuals, with 6% of deaths in 2006 among individuals aged < 50 years, 20% among individuals ages 50-64 years, and 74% among individuals aged ≥ 65 years.^{19,22}

Screening appears to have had considerable impact on reducing CRC incidence and mortality.³⁶ CRC screening was introduced in the 1970s and 1980s, when researchers demonstrated the feasibility of testing for occult blood in stool and initiated randomized clinical trials. In 1985, the diagnosis of colon cancer in President Ronald Reagan increased public awareness of CRC, as demonstrated by a documented increase in the use of tests for early detection of CRC among Medicare recipients and an increase in CRC incidence, particularly for early stage disease.⁷² During 1987-1998, gradual increases in screening for CRC occurred.⁷⁰ Results of randomized clinical trials of FOBT, which demonstrated reductions in both CRC mortality and incidence, provided strong evidence for recommending this test^{73,74}; FOBT continues to be a recommended screening option if performed annually.⁷⁵⁻⁷⁷ Colonoscopy was introduced as a method for screening the entire colon in the 1990s and has been recommended as a screening test for average-risk

individuals aged ≥ 50 years since 1997.⁷⁷ Recent guidelines distinguish between screening tests that primarily detect cancer and those that are more likely to detect both cancer and adenomatous polyps.⁷⁵ Rates of CRC screening have continued to increase from 2000 to 2008, with a marked shift from sigmoidoscopy to colonoscopy for endoscopic screening and a declining use of FOBT (C. Klabunde, unpublished data).^{70,71,78-80}

Research is ongoing regarding the most effective screening methods, individuals most at risk, and optimal surveillance intervals. Simulation models and meta-analyses of published literature have provided insight and potential cost-effective guidelines for policy and health-care. Although the organizations involved in CRC prevention and control have differing recommendations for specific aspects of CRC screening, there is consensus that adults should begin screening at age 50 years, preferably by methods likely to detect cancer and adenomas before they develop into cancer.³⁶ Recent data suggest that approximately 50% of individuals aged ≥ 50 years have been screened according to recommended time intervals (C. Klabunde, unpublished data), with the highest rates of CRC screening ($\approx 60\%$ in 2008) among individuals aged ≥ 65 years. The proportion screened remains $< 70\%$, the rate used by MISCAN-Colon when projecting CRC mortality reductions using optimistic changes in upstream factors; however, rates of colonoscopy screening have increased, whereas rates of FOBT and sigmoidoscopy have declined⁷⁰ (C. Klabunde, unpublished data).

A recent assessment of screening methods indicated that, with high rates of adherence for each method, similar gains in life-years resulted from several screening methods: colonoscopy every 10 years, annual high-sensitivity FOBT, and flexible sigmoidoscopy every 5 years with Hemoccult SENSE (Beckman Coulter, Inc., Miami, Fla) every 2-3 years.³⁶ Also, it has been demonstrated that computed tomographic colonography is potentially as effective as colonoscopy if conducted every 5 years with follow-up for those with polyps ≥ 6 mm.³⁵ Although colonoscopy screening appears to have gained acceptance among healthcare professionals and patients, resources for colonoscopy may limit its use as a primary screening modality.^{78,79} For colonoscopy to be beneficial, downstream resources need to be available to patients who screen positive, including follow-up colonoscopy after positive results of other screening tests, diagnostic colono-

scopy for symptomatic patients, and surveillance colonoscopy after diagnosis of an adenoma or adenocarcinoma. Although risks for adverse events from colonoscopy are low, they increase with age in part because of comorbidities.⁸¹ Some guidelines suggest discontinuing screening of individuals aged > 75 years,⁷⁷ but only approximately 33% of surveyed physicians reported that they stop recommending screening when healthy patients reach a certain age, most commonly at age 80 years.⁸⁰

A family history of CRC and a personal history of CRC, colorectal polyps, or chronic inflammatory bowel disease are major risk factors for CRC.^{82,83} The risk for CRC is approximately twice that of an average individual for those who have a first-degree relative (parent, sibling, or child) who has had CRC; the risk is even greater if the relative was diagnosed at a young age or if more than 1 first-degree relative has had CRC.^{84,85} Individuals with these risk factors may be advised to begin screening before age 50 years, when screening is recommended for average risk individuals. Individuals with certain inherited genetic alterations, such as familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer (also known as Lynch syndrome),⁸⁶ are at even higher risk of developing CRC and should be identified and carefully monitored.⁸⁷

Other major risk factors for CRC that are potentially modifiable include physical inactivity, being overweight and obese, and a diet high in red and processed meats.⁸⁸⁻¹⁰¹ Modification of these risk factors requires behavioral changes that are difficult but important to achieve and impact many health outcomes in addition to CRC. Decreasing the prevalence of these risk factors can be protective against CRC, although changes are expected to result in long-term, not short-term, gains.¹⁰² Changes in community factors and health policy can be important tools for changing individual behaviors. The need for national policy and programs that engage communities in working toward improved nutrition and physical activity, smoking cessation, and decreased alcohol use has been widely recognized. The CDC has proposed a program of 16 community-level initiatives to promote healthy lifestyles through increasing availability of affordable, healthy foods and beverages; encouraging physical activity among youth and adults; and promoting environments that support physical activity. The program fosters partnerships and collaborations to implement the strategies and

evaluate outcomes to assess progress toward a healthier nation.¹⁰³

Continued declines in tobacco use in the United States likely will contribute toward declining trends in CRC incidence. Although neither the 2004 monograph on smoking from the International Agency for Research on Cancer¹⁰⁴ nor the 2004 Surgeon General's report on smoking¹⁰⁵ classified CRC as a smoking-related cancer, consistent evidence demonstrates that smoking increases the development of adenomatous polyps, particularly more aggressive adenomas.¹⁰⁶ Also, increasingly strong and consistent evidence indicates that smoking is associated with CRC, especially with rectal cancer.¹⁰⁷⁻¹⁰⁹ Furthermore, although more research is required to assess the benefits and risks of chemoprevention, use of anti-inflammatory drugs, dietary supplements (eg, calcium), and multivitamins could be protective against this cancer.¹¹⁰⁻¹¹⁴

CRC incidence varies by state and county, presumably because of differences in screening resources and access to care if residence is in an underserved community. One study associates high CRC incidence rates for white and black individuals with residence in counties that had high uninsured or poverty rates, fewer primary physicians, and large proportions of rural or underserved areas.¹¹⁵ However, another US study demonstrated that white individuals living in high-income counties had higher CRC incidence for proximal cancer than those living in middle-poverty or high-poverty counties, suggesting that lifestyle factors such as diet, which is influenced by economic status, play a prominent role in geographic variations in CRC incidence.¹¹⁶

The microsimulation models created by CISNET estimate the extent to which CRC incidence and mortality can be reduced through interventions and treatment and can predict the effects of various scenarios on CRC outcomes. This research indicates that, if 1995-2000 trends for risk factor prevalence, screening, and treatment continue, then death rates from CRC could be reduced by 36% by 2020. However, adverse trends in some risk factors can neutralize gains in others, so gains must be assessed over a long period of time for observed impact.¹⁰² If intervention efforts are successful and increase beyond those of 1995-2000, then deaths from CRC could be substantially reduced. CISNET modeling demonstrates what would be required to reduce the impact of CRC in the

United States. An estimated \$8.4 billion is spent annually on CRC treatment,¹¹⁷ which will increase as CRC prevalence increases to an expected 1.5 million individuals by 2020,¹¹⁸ with most healthcare costs devoted to the initial year after diagnosis.¹¹⁹

Limitations

Cancer surveillance in the United States now covers the majority of the population for monitoring incidence and the entire population for monitoring mortality. However, certain limitations in data sources, data collection, and analyses may have influenced the findings of this report. First, state and national population estimates that were provided by the Census Bureau from 2000 forward and were used initially with statistical reporting last year were developed by using improved and more accurate methodologies, which had noticeable effects on age-specific rates for some counties and states. The net impact of those changes for 2006 was a downward shift in the current postcensus estimates (caused primarily by net international migration estimation) compared with postcensus estimates that were used in the previous report. National incidence rates and death rates were not affected, but some state-level rates were. The NCI also developed modifications to these census estimates in an attempt to account for changes in 2005 county-level populations because of displacement of individuals after hurricanes Katrina and Rita in the most affected counties of Louisiana, Mississippi, Alabama, and Texas.

Second, we used 3 different statistical methods for 2 geographic sets of aggregate data to describe cancer trends: Initially, a single linear regression model was used to describe short-term trends (1997-2006) by race and ethnicity for geographic areas that covered 71% of the United States; next, a joinpoint model was used to describe long-term trends (1975-2006) for all races and ethnicities combined in a subset of these geographic areas that covered approximately 10% of the US population; finally, the AAPC, a new summary measure of a trend over a prespecified fixed interval based on an underlying joinpoint model, was introduced in this report. The joinpoint model is preferable to single linear regression when sufficient numbers of years are available for analysis, because it enables the identification of recent changes in magnitude and direction of trends, although the trends may be

unstable when analyses are based on rates with large variance and when statistical power is low for detecting joinpoint segments. The AAPC can be estimated even if the joinpoint model indicates changes in trends during those years, because this measure is the geometric weighted average of the joinpoint segments over the interval. Enough years of data are now available to use joinpoint analysis for trends by race and ethnicity, and we have used the AAPC based on up to 2 line segments over the 10-year fixed period to report multiple sites and racial and ethnic groups. Methods have yet to be adapted for delayed reporting of aggregated data, except for incidence from the 9 oldest SEER registries. Delayed reporting may affect the most recent joinpoint segment for the national data.

Third, the Veterans Health Administration (VA) hospitals traditionally have been a critical source of data for cancers diagnosed among veterans who are eligible to receive care from these facilities, representing approximately 3% to 8% of cancer diagnoses among men. A 2007 policy change regarding the transfer of VA cancer data to state central cancer registries has resulted in incomplete reporting of VA hospital cases in some registries. This change affected reporting beginning with the third quarter 2004 diagnosis year through the end of the 2006 diagnosis year (available at: http://seer.cancer.gov/csr/1975_2006/results_merged/sect_33_VA_adjustment.pdf accessed on August 21, 2009). Consequently, cancer incidence rates among men for 2005 and 2006 in the SEER 17 registries, which cover >25% of the US population, were underestimated by 1% to 2% for all cancers combined. The level of under reporting varied from 0.5% to 4% according to cancer site, race, and age group.^{13,120} By using similar methods, cancer incidence rates for 2006 among men in the 31 NPCR registries that provided data to the CDC were underestimated between 0.3% to 11.2% (C. Ehemann, unpublished data). The amount of underestimation based on data from other geographic areas may vary by local VA facility reporting patterns and the VA's contribution to the total number of cancers. In late 2008, data-transfer agreements were being established between many VA facilities and states with central registries. Over time, as cancer registries receive these missing VA cases, national cancer incidence estimates will be more complete.

Fourth, assessment of stage-specific CRC incidence trends was limited by a change in methods used to collect information on stage beginning with 2004 diagnoses. The improvements in the use of the Coding System for Collaborative Stage (CS) (available at: <http://www.cancerstaging.org/cstage/index.html> accessed on September 30, 2009) created an artifact in the trend between the 2003 and the 2004 diagnosis years for most state registries funded by the CDC (data not shown). The SEER 9 database was used to estimate stage-specific CRC incidence trends, because the SEER Program has used Extent of Disease since 1988 and CS since 2004 for comparability of information on stage across changes in coding rules.

Fifth, the national estimates of prevalent use of CRC screening and early detection tests were based on trend data from respondents aged ≥ 50 years who participated in the NHIS. These estimates, although they were based on smaller sample sizes with substantially higher response rates than data from the Behavioral Risk Factor Surveillance Survey (BRFSS),¹²¹ tend to be slightly lower than BRFSS estimates.⁷¹ Differences in estimated prevalence may be caused by differences in the mode of administration and response rates from the telephone-based BRFSS compared with the interviewer-administered NHIS. NHIS in-person surveys also provide access to households without telephones and cell-phone-only households, which cannot be reached by means of random-digit-dial surveys, such as that used by the BRFSS. These factors point to the importance of mixed-mode survey methodology and alternative frames for mitigating the increase in telephone survey nonresponse, which erodes coverage of random-digit-dial telephone sampling frames.¹²²

Sixth, as noted routinely in the annual reports,¹⁻¹¹ the broad racial and ethnic groups categorized for our analyses may mask variations in the cancer burden by country of origin, eg, Chinese and Vietnamese in the API group¹²³ and Cubans and Mexicans in the Hispanic group,^{8,124} or by other unique characteristics of high-risk populations.¹²⁵⁻¹²⁸ Also, cancer rates for populations may be limited by difficulties in ascertaining race and ethnicity information from medical records, death certificates, and census reports.¹²⁹

Finally, the MISCAN-Colon model inputs were constrained to those previously used in the published results (available at: <http://cisnet.cancer.gov/projections/>

colorectal accessed on September 30, 2009).²⁹ The current report did not re-examine assumptions concerning risk factors, screening, or treatment interventions, because the perspective was on their relative importance. Additional studies by the MISCAN-Colon modeling group will examine trends in screening modalities as well as other factors that were not incorporated into earlier models. The observed SEER 9 incidence data presented with the MISCAN-Colon model results were adjusted to reflect first primary incidence rates rather than any primary, with adjustments for apparent over reporting of first primary CRC tumors during the early years of the registry using information from the most recent diagnostic years reported in the cancer registries. Minor restrictions in histologic subsites and the exclusion of death-only cases for CRC as reported by SEER were made for the MISCAN-Colon model with little impact on model predictions.

Future Directions

The observed decreases in incidence and death rates from all cancers combined among men and women overall and in nearly all racial and ethnic groups are highly encouraging. This progress must be viewed as part of a long-term strategy for substantial reductions in cancer incidence and mortality through improved risk factors, increased early detection, and better treatment. However, progress has been more limited for some types of cancer for which breakthroughs in prevention, early detection, and treatment remain elusive. Cancer is multifaceted, and many approaches and aspects of this disease affect outcomes for cancer patients. This section summarizes key considerations for future directions in cancer research and interventions.

Microsimulation modeling provides evidence-based support for decisions regarding effective policy and resource allocation for cancer interventions. The models use available data to project outcomes of possible scenarios concerning risk factors, screening, and treatment and are important for decision making when observed data are unavailable or inadequate. For example, CISNET is working on models for prostate cancer to better understand the progression of this leading cause of cancer incidence among men and to assess the benefits of increased prostate screening.^{56,57}

Cancer surveillance systems, which capture prevalence of cancers by age, sex, geographic locations, and other variables, also contribute to informed decision making by enabling an understanding of trends in various aspects of cancer, including diagnosis and treatment. Foundational for cancer prevention and control efforts, the enhancement of cancer registries and surveillance systems can enable a more comprehensive understanding and tracking of cancer and public health and medical interventions.

Many cancers have modifiable risk factors, although risk factor reduction usually results in long-term, not short-term, improvements in cancer incidence. Thus, the impact of changing prevalence of CRC risk factors must be assessed over a long time to observe impact.¹⁰² For example, tobacco prevention efforts over the past decades likely are reflected in recent reductions in lung cancer incidence. Also, research demonstrates that states with comprehensive tobacco-control programs have more rapid decreases in lung cancer than states without such programs.^{130,131} Although much can be learned from the policy and program strategies used in comprehensive tobacco control, expanded current research is needed on the importance of lifestyle behaviors, particularly physical inactivity, poor diet, and obesity, to cancer risk and survival.¹³²⁻¹³⁴ Extensive behavioral research, including randomized controlled trials, has demonstrated that individually focused behavioral interventions result in recommended changes in these health behaviors. However, a key challenge is to identify what is needed to ensure that these behavioral changes are sustained. Research has identified that changes in the environments and policies that support recommended health behaviors are important to achieve and sustain beneficial lifestyle behaviors. Being overweight and failing to exercise are adverse trends that appear to increase risk for CRC,⁸⁹⁻⁹² especially colon cancer.^{95,96,98,135} An estimated 33% of US adults are overweight, and another 34% are obese.¹⁰³ Increasing CRC incidence among young adults (aged <50 years) may be an early indicator of the adverse impact of these risk factors. The CDC recently published policy and communication strategies to decrease obesity and physical inactivity,¹⁰³ including recommended policies to facilitate better nutrition and environments conducive to physical activities such as walking or biking. In 2009, a Weight of the Nation conference¹³⁶ addressed the need for multiple

approaches to curbing obesity-related illness¹³⁷ and containing the rising cost of obesity for the nation, which was estimated at \$147 billion in 2007.¹³⁸

Several risk factors associated with cancer appear to act over a long time, although some changes in risk factors can impact cancer incidence in a shorter period of time. One example is the decline in breast cancer in 2002 after lower use of combined hormone therapy among women.¹³⁹⁻¹⁴¹ Beyond risk factor reduction, chemoprevention is a growing research area, especially because several medications used for other purposes appear to be protective against CRC; however, some substances such as aspirin have adverse side effects, so additional research is needed to clarify the effectiveness, appropriate dose, and potential toxicity of potential chemopreventive therapies.¹¹⁰⁻¹¹² Recent concerns also are focused on an increased risk of CRC¹⁴² from nationwide fortification of cereal grains with folic acid in the late 1990s to reduce neural tube birth defects.

Disparities in cancer incidence and mortality need further investigation, including ways to decrease disparities related to race or ethnicity, socioeconomic status, insurance status, geographic location, and access to healthcare. Eliminating these disparities will require increased access to screening and advanced treatment modalities, which place demands on healthcare delivery systems. Short-term and long-term impact on the healthcare provider workforce, facilities and technology, and financial resources for cancer interventions to improve health outcomes for all segments of the population must be considered. Modifiable risk factors have been identified (eg, obesity, poor diet, alcohol consumption, and lack of physical activity) that require effective culturally sensitive interventions targeting specific populations to reduce these risk factors.

CRC has been the highlight of this report. Although great progress has been made in reducing the impact of CRC, improved application of currently available knowledge and ongoing research are needed to make further inroads. CRC research priorities were established by the NCI Progress Review Group and have guided a decade of activities, including biologic and etiologic research in CRC.¹⁴³ Genome-wide association studies recently have implicated multiple loci across the genome that may contribute to CRC susceptibility.¹⁴⁴

Research also is needed to enhance screening technologies as well as strategies to increase screening and early detection; such strategies include community and agency collaborations to implement screening,¹⁴⁵ enhanced screening in primary care settings and rural areas,¹⁴⁶ and removal of cultural and language barriers to screening.¹⁴⁶ Screening has increased considerably since 2000, yet only approximately 50% of adults aged ≥ 50 years were screened in 2005.⁷¹ Studies have suggested possible reasons for less-than-optimal use of CRC screening, including variability in physicians' interpretation and use of CRC screening guidelines⁸⁰; lack of insurance coverage, regular health provider, or awareness⁷¹; and a slight increase in adverse events associated with colonoscopy as the age of screened patients increases.⁸¹ The CDC's new Colorectal Cancer Control program will provide direct screening services to populations at greatest need and will focus attention on increasing CRC screening rates among the US population aged ≥ 50 years nationwide (available at: www.cdc.gov/cancer/colorectal and www.cdc.gov/screenforlife accessed on October 6, 2009).

Several public, private, and voluntary organizations have targeted CRC screening as one of their most important cancer-control priorities and have been working to educate the public and medical providers concerning the importance of screening.¹⁴⁷ Advocacy efforts at the state and federal levels have encouraged state legislation requiring coverage for the full range of CRC screening tests and the development of federal programs to enhance access to screening and treatment of medically underserved populations. A state-of-the-science conference hosted by the NIH in 2010 will focus on ways to enhance the use and quality of CRC screening.¹⁴⁸ Also, a CDC-CISNET collaboration is working to assess the capacity of the US healthcare system to increase CRC screening of individuals ages 50-64 years and to determine cost implications for Medicare, Medicaid, and private payors, taking into consideration increased costs for early detection yet savings in treatment costs.

Researchers also have made great strides in developing treatment regimens to optimize patient response and performance, particularly for patients with metastatic CRC. Some treatments that have positively impacted morbidity, quality of life, and survival for CRC patients include multimodality therapy for rectal cancer and the use of surgical approaches that result in higher rates of

sphincter preservation.¹⁴⁹ Also, surgical resection of hepatic metastases and, more recently, the development of new chemotherapies appear to increase survival for patients with metastatic disease.^{150,151} Targeted therapies with monoclonal antibodies have been developed¹⁵² as well as more individualized CRC therapies based on genetic characteristics of the patient's tumor.¹⁵³ A CRC patient's survival and quality of life depend on treatment decisions, and improved treatments and optimal combination of therapies continue to be goals.¹⁵⁴ Some patients do not tolerate chemotherapy well, and enhanced quality-of-life research is needed for CRC patients, including palliative care. Best practices for treatments based on a patient's needs, staging, preferences, and performance status (response to chemotherapy) need to be promoted and adopted. Research into treatment options that result in even small gains in CRC patient survival and performance requires large clinical trials before the treatment can be made available for general use,¹⁵⁴ so ways to facilitate cancer drug approval also are needed.¹⁵⁵

Disparities exist for CRC as well. Men have higher rates than women, and black individuals have higher rates than other racial/ethnic groups. Geographic disparities also have been reported and may be influenced by access to healthcare and screening (in low-poverty areas) and by lifestyle factors (in high-poverty and urban areas).^{116,156} Studies also indicate that black patients with CRC are diagnosed more often at late stages and less often receive standard therapies than white patients¹⁵⁷; they also have less follow-up surveillance¹⁵⁸ and poorer survival rates.¹⁵⁹ More research is needed regarding the systemic, clinical, social, cultural, biologic, environmental, and behavioral factors that influence CRC incidence, mortality, and disparities.

Although much progress can be achieved by applying better what we already know about cancer causation, prevention, and treatment (eg, tobacco control, vaccination for human papillomavirus, chemoprevention of breast cancer in high-risk groups), more research is needed across the spectrum of cancers in all areas: prevention, early detection, treatment, and palliation. Further etiologic research is needed for particularly lethal cancer sites (eg, pancreatic), those with unexplained increased incidence (ie, cancers of the thyroid, liver, pancreas, kidney, and melanoma) (Table 4), and cancers for which limited progress has been made. Extensive research efforts also are

needed to develop personalized/targeted cancer therapies that involve a better understanding of the genetic and epigenetic changes that occur in cells during progression to cancer, the molecular composition of cancer subtypes, gene expression, and proteomics.¹⁶⁰⁻¹⁶³ A combination of policy, healthcare service delivery, communication, and engineering and technology interventions can further reduce the impact of cancer.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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