

# Trends in cancer incidence and mortality rates in the United States from 1975 to 2016

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**Background:** Cancer is the second leading cause of death in the United States (US). The goal of this study was to characterize the trends in cancer incidence and mortality in the US from 1975 to 2016.

**Methods:** In this study, we analyzed 4,711,958 cancer cases and 21,489,462 cancer death cases from the Surveillance, Epidemiology and End Results (SEER) database. Cancer incidence and mortality were assessed according to sex, race, and age group. Cancer survival rates between 2010 and 2016 were also examined.

**Results:** The continuous decline in the overall cancer mortality rate from the early 1990s has resulted in overall decreases of 33.6% and 23.6% in the cancer mortality rates of males and females, respectively. In males, the top three leading cancers and causes of cancer death from 1975 to 2016 were prostate, lung and bronchial, and colon and rectal cancers, while in females, the top three leading cancers and causes of cancer death from 1975 to 2016 were prostate, lung and bronchial, and colon and rectal cancers, while in females, the top three leading cancers and causes of cancer death from 1979 to 2016 were breast, lung and bronchial, and colon and rectal cancers. The 5-year relative survival rates of males and females for all cancers combined, diagnosed from 2010–2016, were 68.5% and 70.1%, respectively. The overall cancer incidence and mortality were higher in males than females from 1975–2016. Also, black people had higher mortality and shorter survival rates for all cancers combined compared with white people (in both sexes).

**Conclusions:** This study presents a comprehensive overview of cancer incidence and mortality in the US over the past 42 years. Such information can provide a scientific basis for cancer prevention and control.

Keywords: Cancer incidence; cancer mortality; cancer survival rates; lung cancer; breast cancer; prostate cancer

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## Introduction

Cancer is the second leading cause of death after heart disease in the United States (US) (1,2). In 2019, it was estimated that there were 1,762,450 new cancer cases and 606,880 cancer deaths in the US (2). Considerable progress in the prevention, detection, diagnosis, and treatment of cancer has been achieved over the past four decades. An understanding of the trends in cancer incidence and mortality rates is critical for continued advancement. However, few studies have systematically documented these changes (1-3). In this article, we analysed age-adjusted cancer incidence and mortality rates between 1975 and 2016 in the US. In addition, we also analysed cancer survival rates between 2010 and 2016. This information will provide valuable insights into cancer prevention and control at the national level.

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# Methods

# Cancer incidence, mortality, and survival data

The Surveillance, Epidemiology and End Results (SEER) database is an open-access resource for cancer-based epidemiology and survival analyses. Cancer incidence and survival data were obtained from the SEER database of Incidence-SEER 9 Regs Research Data, November 2018 Sub [1975–2016] <Katrina/Rita Population Adjustment>. A total of 4,711,958 cancer cases spanning 1975–2016 are registered within the nine oldest SEER areas (Connecticut, Hawaii, Iowa, New Mexico, Utah, and the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland and Seattle-Puget Sound), representing approximately 9% of the US population.

The US mortality data, collected and maintained by the National Centre for Health Statistics (NCHS), can be analysed using the SEER\*Stat software. The NCHS granted the SEER program limited permission to provide mortality data to the public. Cancer mortality data were collected from the SEER database of Mortality-All cause of death (COD), Aggregated Total US [1969–2016] <Katrina/ Rita Population Adjustment>. The underlying mortality data were provided by the NCHS (www.cdc.gov/nchs). A total of 21,489,462 cancer death cases spanning 1975–2016 are registered in this database.

All cancer cases were classified according to the Site Recode ICD-O-3/World Health Organization (WHO) 2008 (2).

Ethical approval for this study was exempted by the Medical Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University (Hangzhou, China), as SEER is a publicly available database, and the data extracted from SEER were identified as belonging to a non-human study. All patient data were anonymized.

## Statistical analysis

All cancer incidence and mortality rates and 95% confidence intervals (CI) were age-adjusted using the 2000 US standard population and expressed per 100,000 personyears (2,4). Annual rates are shown graphically as trends. Temporal trends in cancer incidence and mortality rates were examined, and separate analyses were conducted for males and females. We also calculated the age-adjusted cancer incidence and mortality rates according to race/ ethnicity (white, black, other) and age group (birth–39, 40–49, 50–59, 60–69, and  $\geq$ 70 years) (5,6). Cancer survival rates between 2010 and 2016 were also examined according to sex and race/ethnic group. All data analyses were performed using SEER\*Stat software version 8.3.5 (2,4).

# **Results**

#### Trends in cancer incidence

The age-adjusted incidence rate and percentage changes from 1975-2016 of the 20 leading cancers by sex in the US in 2016 are shown in Table 1. The overall cancer incidence rate in males decreased by 28.7%, from a maximal peak of 658.4 (per 100,000 population) in 1992 to 469.2 (per 100,000 population) in 2016, and this decline continues to date. In females, this number has been relatively stable since its maximal peak of 434.3 (per 100,000 population) in 1998 to 411.5 (per 100,000 population) in 2016 (Figure 1). From 1975-2016, the overall cancer incidence was higher for males than females (Figure 1). In males, the overall cancer incidence reached a distinct peak in 1992, mainly due to prostate cancer (Figure 1). The top five malignant cancers in males in 2016 were prostate, lung and bronchial, colon and rectal, and urinary bladder cancers, as well as melanoma of the skin (Table 1; Figure 2A). Similarly, the top five malignant cancers in females in 2016 were breast, lung and bronchial, colon and rectal, corpus and uterus, and thyroid cancers (Table 1; Figure 2B).

From 1975–2016 (for males) and 1979–2016 (for females), the top three leading malignancies were prostate (men), breast (women), lung and bronchial, and colon and rectal cancers (*Figure 2*). From 1975–2016, prostate and breast cancers were the main cancers in males and females, respectively (*Figure 2*). The incidence rate of prostate cancer (per 100,000 population) increased from 94.0 in 1975 to a maximal peak of 237.5 in 1992, and then declined to 108.4 in 2016 (*Figure 2A*). Similarly, the incidence rate (per 100,000 population) for breast cancer in females increased from 105.1 in 1975 to a maximal peak of 141.6 in 1999, and subsequently decreased to 126.5 in 2016 (*Figure 2B*).

Lung and bronchial cancers remained the second leading cancer in males from 1975 to 2016, and in females from 1992 to 2016, respectively. The incidence rate (per 100,000 population) of lung and bronchial cancers in males declined by 44.1%, from a maximal peak of 102.0 in 1984 to 57.0 in 2016 (*Figure 2A*). However, in females, it declined gradually after reaching a maximal peak of 53.8 in 2005, falling to 45.1 in 2016 (*Figure 2B*).

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	Inci	dence	rank	Age-adj	usted incidence rate (	95% CI)	Incid	lence co	ount	Relative change	Relative change
Cancer	1975	2000	2016	1975	2000	2016	1975	2000	2016	in incidence (2016 vs. 1975)	in incidence (2016 vs. 2000)
Male											
All malignant cancers				466.8 (461.5–472.2)	581.1 (576.5–585.7)	469.2 (465.8–472.6)	33,059	64,015	75,836	0.5%	-19.3%
Prostate	-	÷	-	94.0 (91.5–96.6)	183.3 (180.8–185.9)	108.4 (106.8–110.0)	5,802	19,945	18,713	15.3%	-40.9%
Lung and bronchus	2	2	2	89.5 (87.3–91.8)	82.1 (80.4–83.9)	57.0 (55.8–58.3)	6,738	8,862	8,962	-36.3%	-30.6%
Colon and rectum	ю	ო	ო	68.4 (66.4–70.6)	63.7 (62.2–65.3)	42.5 (41.4–43.5)	4,639	6,844	6,772	-37.9%	-33.3%
Urinary bladder	4	4	4	34.4 (32.9–35.9)	38.8 (37.6–40.0)	33.5 (32.6–34.5)	2,319	4,095	5,101	-2.6%	-13.7%
Melanoma of the skin	#	9	5	8.5 (7.9–9.2)	24.0 (23.1–24.9)	32.0 (31.1–32.9)	690	2,783	5,056	276.5%	33.3%
Lymphoma	7	5	9	16.8 (15.8–17.7)	27.6 (26.7–28.6)	26.4 (25.6–27.2)	1,363	3,191	4,121	57.1%	-4.3%
Kidney and renal pelvis	б	œ	7	10.3 (9.6–11.1)	17.5 (16.8–18.3)	21.2 (20.5–22.0)	791	1,984	3,459	105.8%	21.1%
Leukaemia	9	7	œ	16.9 (15.9–18.0)	17.9 (17.2–18.8)	17.9 (17.2–18.6)	1,210	1,995	2,782	5.9%	0.0%
Pancreas	8	0	0	15.6 (14.7–16.6)	13.3 (12.6–14.0)	14.3 (13.7–14.9)	1,085	1,444	2,269	-8.3%	7.5%
Liver	16	14	10	3.7 (3.2–4.2)	7.3 (6.8–7.8)	11.4 (10.9–11.9)	275	840	2,003	208.1%	56.2%
Myeloma	14	13	1	6.4 (5.8–7.1)	7.7 (7.1–8.2)	8.6 (8.2–9.1)	448	832	1,369	34.4%	11.7%
Stomach	Ŋ	10	12	17.1 (16.1–18.2)	11.7 (11.1–12.4)	8.5 (8.1–9.0)	1,156	1,253	1,334	-50.3%	-27.4%
Thyroid	19	17	13	3.1 (2.7–3.5)	4.0 (3.7–4.4)	7.5 (7.1–8.0)	262	505	1,200	141.9%	87.5%
Brain and other nervous system	12	1	14	6.8 (6.3–7.4)	8.2 (7.7–8.8)	7.4 (6.9–7.8)	603	991	1,165	8.8%	-9.8%
Oesophagus	12	12	14	6.8 (6.2–7.4)	8.0 (7.5–8.5)	7.4 (7.0–7.8)	512	893	1,210	8.8%	-7.5%
Testis	16	16	16	3.7 (3.3–4.1)	5.7 (5.4–6.2)	6.2 (5.8–6.6)	363	794	921	67.6%	8.8%
Tongue	18	18	17	3.4 (3.0–3.8)	3.8 (3.4–4.1)	5.6 (5.2–6.0)	265	451	970	64.7%	47.4%
Larynx	10	14	18	9.5 (8.8–10.2)	7.3 (6.8–7.8)	4.7 (4.3–5.0)	755	826	768	-50.5%	-35.6%
Soft tissue including heart	20	19	19	2.7 (2.3–3.1)	3.6 (3.3–4.0)	4.2 (3.9–4.6)	221	430	649	55.6%	16.7%
Tonsil	24	20	20	1.7 (1.4–2.1)	2.3 (2.0–2.6)	3.4 (3.1–3.7)	135	280	599	100.0%	47.8%
Table 1 (continued)											

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Cancer			rank	Age-adju	sted incidence rate (	95% CI)	Inck	dence cc	ount	Relative change	Helative change
	1975	2000	2016	1975	2000	2016	1975	2000	2016	in incidence (2016 vs. 1975)	in incidence (2016 vs. 2000)
Female											
All malignant cancers				365.9 (362.0–369.8)	422.7 (419.3–426.1)	411.5 (408.4–414.5)	34,302	59,432	75,473	12.5%	-2.6%
Breast	÷	-	÷	105.1 (103.0–107.2)	136.6 (134.7–138.6)	129.8 (128.1–131.5)	9,657	18,970	23,596	23.5%	-5.0%
Lung and bronchus	4	2	2	24.5 (23.5–25.5)	51.2 (50.0–52.4)	45.1 (44.1–46.1)	2,349	7,170	8,616	84.1%	-11.9%
Colon and rectum	N	с	с	53.7 (52.2–55.2)	46.8 (45.7–47.9)	33.2 (32.4–34.1)	4,962	6,776	6,157	-38.2%	-29.1%
Corpus and uterus	ю	4	4	35.5 (34.3–36.7)	24.8 (24.0–25.7)	27.9 (27.1–28.7)	3,493	3,436	5,372	-21.4%	12.5%
Thyroid	13	80	5	6.5 (5.9–7.0)	11.1 (10.6–11.7)	21.3 (20.6–22.0)	617	1,531	3,453	227.7%	91.9%
Melanoma of the skin	12	9	9	7.4 (6.9–8.0)	15.5 (14.9–16.2)	20.5 (19.8–21.2)	700	2,159	3,617	177.0%	32.3%
Lymphoma	7	5	7	12.0 (11.3–12.7)	18.5 (17.8–19.2)	18.2 (17.6–18.9)	1,161	2,618	3,325	51.7%	-1.6%
Pancreas	6	10	œ	9.1 (8.5–9.8)	9.8 (9.3–10.4)	11.6 (11.2–12.2)	849	1,423	2,247	27.5%	18.4%
Leukaemia	ω	б	6	10.0 (9.3–10.6)	10.7 (10.2–11.3)	10.4 (9.9–10.9)	940	1,527	1,871	4.0%	-2.8%
Kidney and renal pelvis	15	12	0	4.5 (4.1–5.0)	8.5 (8.1–9.0)	10.4 (9.9–10.9)	430	1,195	1,915	131.1%	22.4%
Ovary	5	7	1	16.3 (15.5–17.2)	14.4 (13.7–15.0)	10.1 (9.7–10.6)	1,537	2,003	1,851	-38.0%	-29.9%
Urinary bladder	10	11	12	8.9 (8.3–9.5)	9.6 (9.1–10.1)	8.3 (7.9–8.7)	824	1,383	1,587	-6.7%	-13.5%
Cervix uteri	9	13	13	14.8 (14.0–15.6)	7.7 (7.3–8.2)	6.4 (6.0–6.8)	1,364	1,073	1,029	-56.8%	-16.9%
Myeloma	16	16	14	3.9 (3.5–4.3)	5.0 (4.7–5.4)	5.7 (5.3–6.0)	361	719	1,080	46.2%	14.0%
Stomach	5	15	15	7.8 (7.3–8.4)	5.4 (5.0–5.8)	5.0 (4.7–5.4)	715	790	933	-35.9%	-7.4%
Brain and other nervous system	14	14	15	5.0 (4.6–5.5)	5.7 (5.3–6.1)	5.0 (4.7–5.3)	499	784	863	0.0%	-12.3%
Liver	22	18	17	1.5 (1.3–1.8)	2.5 (2.2–2.8)	3.4 (3.1–3.7)	141	355	664	126.7%	36.0%
Soft tissue including heart	20	17	18	1.8 (1.6–2.1)	2.6 (2.3–2.8)	2.9 (2.6–3.1)	176	353	491	61.1%	11.5%
Vulva	18	19	19	2.1 (1.8–2.4)	2.3 (2.0–2.5)	2.5 (2.2–2.7)	197	324	464	19.0%	8.7%
Tongue	25	21	20	1.2 (1.0–1.4)	1.5 (1.3–1.7)	2.2 (2.0–2.4)	115	212	414	83.3%	46.7%
Small intestine	27	24	20	0.9 (0.8–1.2)	1.4 (1.2–1.6)	2.2 (2.0–2.5)	89	192	414	144.4%	57.1%



**Figure 1** Trends in overall cancer incidence and mortality rates by sex in the United States [1975–2016]. Rates are age-adjusted to the 2000 United States standard population.

The incidence rate of the third leading cancer (colon and rectal) decreased in both males and females (*Figure 2*). In males, the incidence rate (per 100,000 population) for colon and rectal cancer decreased by 46.3%, from a maximal peak of 79.2 in 1985 to 42.5 in 2016, while in females, the incidence rate fell by 42.1%, from a maximal peak of 57.3 in 1985 to 33.2 in 2016 (*Figure 2*).

The changes in the age-adjusted incidence rate of different races and ethnicities from 1975–2016 were also analysed (Tables S1 and S2; Figures S1-S3). The overall cancer incidence rate was higher in black males compared to white males from 1975 to 2016, but exhibited the opposite trend in females over the same time period (Figure S1). The changes in the age-adjusted incidence rate of different age groups from 1975–2016 were also examined (Tables S3-S7; Figures S4 and S5).

## Trends in cancer mortality

Age-adjusted mortality and percentage changes from 1975–2016 of the 20 leading causes of cancer death by sex in the US in 2016 are shown in *Table 2*. In males, the overall cancer mortality rate fell by 33.6%, from a maximal peak of 279.8 (per 100,000 population) in 1990 to 185.9

(per 100,000 population) in 2016. Similarly, this rate also decreased in females by 23.6%, from a maximal peak of 175.3 (per 100,000 population) in 1991 to 134.0 (per 100,000 population) in 2016 (*Figure 1*). Moreover, this downward trend continues to date, irrespective of sex. From 1975–2016, the overall cancer mortality rate was higher in males than females (*Figure 1*). In 2016, malignant cancers of the lung and bronchus, prostate, colon and rectum, and pancreas, as well as leukaemia were the five leading causes of cancer death in males (*Figure 3A*; *Table 2*), while in females, the same trend occurred, except that prostate cancer and leukaemia were replaced by breast and ovarian cancers, respectively (*Figure 3B*; *Table 2*).

From 1975–2016, the top three leading causes of cancer death were lung and bronchial, prostate (men), breast (women), and colon and rectal cancers (Figure 3). Although the mortality (per 100,000 population) for lung and bronchial cancer in males dropped by 48.2%, from a maximal peak of 90.6 in 1990 to 46.9 in 2016, and similarly decreased in females by 23.3%, from a maximal peak of 41.6 in 2002 to 31.9 in 2016, it remained the leading cause of cancer death in males from 1975 to 2016 and in females from 1987 to 2016 (Figure 3). Prostate cancer mortality (per 100,000 population) fell by 50.6%, from a maximal peak of 39.3 in 1991 to 19.4 in 2016, yet remained the second leading cause of cancer death in males from 1981 to 2016 (Figure 3A). Breast cancer mortality (per 100,000 population) declined by 39.8%, from a maximal peak of 33.2 in 1988 to 20.0 in 2016, but remained the second leading cause of cancer death in females from 1988 to 2016 (Figure 3B). For colon and rectal cancer, the mortality (per 100,000 population) dropped by 51.6% in males, from a maximal peak of 33.7 in 1978 to 16.3 in 2016, and by 54.7% in females, from a maximal peak of 25.4 in 1976 to 11.5 in 2016. Despite this decline, it remained the third leading cause of cancer death from 1981 to 2016 in both sexes (Figure 3).

Furthermore, the changes in the age-adjusted mortality rate of different races and ethnicities from 1975–2016 were analysed (Figures S1,S6,S7; Tables S8 and S9). From 1975–2016, the overall cancer mortality rate was higher for blacks compared to whites in both sexes (Figure S1). In addition, the changes in the age-adjusted mortality rate of different age groups from 1975–2016 were also analysed (Figures S8 and S9; Tables S10-S14).

## Cancer survival

Table 3 shows the 5-year relative survival rates by sex and

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Figure 2 Trends in the incidence rate of the 10 leading cancers by sex in the United States [1975–2016]. Rates are age-adjusted to the 2000 United States standard population. (A) Male; (B) female.

race/ethnicity for the 20 leading cancers [2016] diagnosed between 2010 and 2016. Among these, cancers of the brain and other nervous system (31.8%), stomach (29.8%), liver (21.2%), oesophagus (20.8%), lung and bronchus (17.4%) and pancreas (10.5%) in males, and cancers of the ovary (48.5%), stomach (35.8%), brain and other nervous system (35.2%), lung and bronchus (24.6%), liver (23.3%) and pancreas (9.5%) in females, displayed 5-year relative survival rates of less than 50%. The 5-year relative survival rate for all cancers combined, diagnosed between 2010 and 2016, was higher in females (70.1%) than males (68.5%)(Table 3). Also, the 5-year relative survival rate for all cancers combined in males and females was 69.3% and 71.2% in whites, 65.6% and 61.3% in blacks, and 58.5% and 69.3% in other, respectively (Table 3). Black people had a lower 5-year survival rate than white people for 17 (in males) and

16 (in females) of the 20 leading cancers (*Table 3*).

In addition, the analysis of the 1- and 3-year relative survival rates by sex and race/ethnicity for the 20 leading cancers (2016) diagnosed between 2010 and 2016 is shown in Tables S15,S16.

#### Discussion

A total of 4,711,958 cancer cases spanning 1975–2016 are registered in the nine oldest SEER areas, representing approximately 9% of the US population. From 1975–2016, a total of 21,489,462 cancer death cases were recorded in the US. This vast amount of data provides an accurate reflection of the actual cancer incidence and mortality rates in the US. In males, the overall cancer incidence rate (per 100,000 population) declined by 28.7%, from a maximal

Lade 2 Mortanty rate chang		rtality	/ rank	n the 20 leading causes of Ade-adi	usted mortality rate (9	In the United States	Ď	eath count		Relative	Relative
All causes	1975	200	0 2016	1975	2000	2016	1975	2000	2016	change in mortality (2016 vs. 1975)	change in mortality (2016 <i>v</i> s. 2000)
Male											
All malignant cancers				258.4 (257.2–259.6)	248.5 (247.5–249.4)	185.9 (185.2–186.6)	198,586	286,072	314,568	-28.1%	-25.2%
Lung and bronchus	-	-	÷	76.4 (75.8–77.0)	76.5 (76.0–77.0)	46.9 (46.6–47.3)	63,297	90,410	80,775	-38.6%	-38.7%
Prostate	ო	N	2	31.0 (30.5–31.4)	30.4 (30.1–30.7)	19.4 (19.2–19.6)	19,426	31,078	30,370	-37.4%	-36.2%
Colon and rectum	N	С	С	32.8 (32.4–33.3)	25.1 (24.8–25.4)	16.3 (16.1–16.5)	23,819	28,484	27,642	-50.3%	-35.1%
Pancreas	4	4	4	13.8 (13.5–14.1)	12.1 (11.9–12.3)	12.7 (12.5–12.8)	10,606	14,237	21,899	-8.0%	5.0%
Leukaemia	9	9	5	11.0 (10.7–11.2)	10.3 (10.1–10.5)	8.3 (8.1–8.4)	8,382	11,803	13,360	-24.5%	-19.4%
Liver	12	÷	9	3.7 (3.6–3.8)	5.7 (5.5–5.8)	7.7 (7.6 –7.9)	2,917	6,843	14,458	108.1%	35.1%
Urinary bladder	7	8	7	9.8 (9.5–10.0)	7.6 (7.4–7.8)	7.5 (7.4–7.7)	6,604	8,163	11,941	-23.5%	-1.3%
Lymphoma	80	5	œ	8.6 (8.4–8.8)	10.8 (10.6–10.9)	7.3 (7.1–7.4)	7,082	12,498	11,879	-15.1%	-32.4%
Oesophagus	0	7	0	6.4 (6.2–6.5)	7.7 (7.5–7.9)	7.0 (6.8–7.1)	5,196	9,279	12,317	9.4%	-9.1%
Brain and other nervous system	÷	10	10	5.0 (4.8–5.1)	5.6 (5.4–5.7)	5.5 (5.4–5.6)	4,543	7,011	9,510	10.0%	-1.8%
Kidney and renal pelvis	10	10	11	5.2 (5.0–5.3)	6.1 (6.0–6.3)	5.2 (5.1–5.4)	4,199	7,249	8,996	0.0%	-14.8%
Myeloma	12	Ē	12	3.7 (3.6–3.8)	4.7 (4.5–4.8)	4.1 (4.0–4.2)	2,830	5,321	6,734	10.8%	-12.8%
Stomach	Ŋ	6	13	12.3 (12.0–12.5)	6.4 (6.2–6.5)	4.0 (3.9–4.1)	8,954	7,328	6,845	-67.5%	-37.5%
Melanoma of the skin	15	14	14	2.6 (2.5–2.8)	3.8 (3.7–3.9)	3.2 (3.2–3.3)	2,193	4,592	5,425	23.1%	-15.8%
Intrahepatic bile duct	41	18	3 15	0.1 (0.1–0.2)	1.1 (1.1–1.2)	2.0 (1.9–2.0)	117	1,333	3,385	1900.0%	81.8%
Non-melanoma skin	17	17	16	1.3 (1.2–1.4)	1.4 (1.4–1.5)	1.8 (1.7–1.8)	868	1,597	2,871	38.5%	28.6%
Larynx	14	10	17	3.3 (3.2–3.5)	2.5 (2.5–2.6)	1.7 (1.6–1.8)	2,739	3,041	3,048	-48.5%	-32.0%
Soft tissue including heart	20	16	3 18	1.0 (0.9–1.1)	1.5 (1.4–1.6)	1.5 (1.4–1.6)	855	1,842	2,518	50.0%	0.0%
Tongue	16	10	19	1.6 (1.5–1.7)	0.9 (0.8–1.0)	1.0 (1.0–1.1)	1,321	1,115	1,858	-37.5%	11.1%
Bones and joints	20	21	20	1.0 (1.0–1.1)	0.5 (0.5–0.6)	0.6 (0.5–0.6)	908	682	914	-40.0%	20.0%
Table 2 (continued)											

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	Mor	tality r	ank	Age-adj	usted mortality rate (	95% CI)	ŏ	eath couni	Ţ	Relative	Relative
All causes	1975	2000	2016	1975	2000	2016	1975	2000	2016	change in mortality (2016 vs. 1975)	change in mortality (2016 vs. 2000)
Female											
All malignant cancers				160.0 (159.2–160.8)	166.7 (166.1–167.3)	134.0 (133.4–134.5)	165,509	267,008	283,463	-16.3%	-19.6%
Lung and bronchus	ო	-	-	17.6 (17.3–17.8)	41.1 (40.8–41.4)	31.9 (31.7–32.2)	18,584	65,016	68,094	81.3%	-22.4%
Breast	÷	N	2	31.4 (31.1–31.8)	26.6 (26.4–26.9)	20.0 (19.8–20.2)	32,158	41,872	41,487	-36.3%	-24.8%
Colon and rectum	2	ო	с	25.0 (24.6–25.3)	17.5 (17.3–17.7)	11.5 (11.4–11.7)	25,553	28,950	24,644	-54.0%	-34.3%
Pancreas	5	4	4	8.4 (8.2–8.6)	9.3 (9.1–9.4)	9.7 (9.6–9.8)	8,831	15,094	20,858	15.5%	4.3%
Ovary	4	S	5	9.8 (9.6–10.0)	8.9 (8.7–9.0)	6.8 (6.6–6.9)	10,340	14,060	14,223	-30.6%	-23.6%
Corpus and uterus	10	ø	9	5.3 (5.1–5.4)	4.1 (4.0–4.2)	5.0 (4.9–5.1)	5,570	6,585	10,733	-5.7%	22.0%
Leukaemia	9	7	7	6.2 (6.0–6.3)	5.9 (5.8–6.0)	4.7 (4.7–4.8)	6,372	9,594	9,927	-24.2%	-20.3%
Lymphoma	œ	9	8	5.6 (5.5–5.8)	7.1 (7.0–7.2)	4.4 (4.3–4.5)	5,907	11,518	9,389	-21.4%	-38.0%
Brain and other nervous system	5	6	Ø	3.4 (3.3–3.5)	3.7 (3.6–3.8)	3.6 (3.5–3.7)	3,667	5,644	7,324	5.9%	-2.7%
Myeloma	13	10	10	2.4 (2.3–2.5)	3.3 (3.2–3.4)	2.6 (2.5–2.6)	2,552	5,318	5,532	8.3%	-21.2%
Liver	15	15	11	2.0 (1.9–2.0)	2.1 (2.0–2.1)	2.5 (2.4–2.6)	2,017	3,349	5,397	25.0%	19.0%
Kidney and renal pelvis	13	12	12	2.4 (2.3–2.5)	2.8 (2.7–2.9)	2.3 (2.2–2.3)	2,547	4,487	4,846	-4.2%	-17.9%
Stomach	7	1	13	5.9 (5.8–6.1)	3.2 (3.1–3.3)	2.2 (2.1–2.3)	6,025	5,317	4,588	-62.7%	-31.3%
Cervix uteri	ø	12	13	5.6 (5.4–5.7)	2.8 (2.7–2.9)	2.2 (2.2–2.3)	5,550	4,200	4,188	-60.7%	-21.4%
Urinary bladder	12	14	15	2.8 (2.7–2.9)	2.3 (2.2–2.3)	2.1 (2.1–2.2)	2,765	3,839	4,705	-25.0%	-8.7%
Intrahepatic bile duct	36	19	16	0.1 (0.1–0.1)	0.9 (0.8–0.9)	1.6 (1.5–1.6)	63	1,391	3,329	1500.0%	77.8%
Oesophagus	16	16	17	1.7 (1.6–1.8)	1.8 (1.8–1.9)	1.5 (1.4–1.5)	1,801	2,953	3,142	-11.8%	-16.7%
Melanoma of the skin	18	16	18	1.6 (1.5–1.7)	1.8 (1.7–1.9)	1.3 (1.3–1.4)	1,602	2,828	2,763	-18.8%	-27.8%
Soft tissue including heart	20	18	19	0.8 (0.8–0.9)	1.2 (1.1–1.3)	1.2 (1.1–1.2)	858	1,854	2,301	50.0%	0.0%
Gallbladder	16	19	20	1.7 (1.7–1.8)	0.9 (0.8–0.9)	0.7 (0.6–0.7)	1,798	1,385	1,463	-58.8%	-22.2%



Figure 3 Trends in the mortality rate of the 10 leading causes of cancer death by sex in the United States [1975–2016]. Rates are ageadjusted to the 2000 United States standard population. (A) Male; (B) female.

peak of 658.4 in 1992 to 469.2 in 2016, and this trend continues to date (*Figure 1*). However, in females, this rate has been relatively stable since its maximal peak of 434.3 in 1998, only decreasing to 411.5 in 2016 (*Figure 1*). The overall cancer incidence in males showed a distinct peak in 1992, predominantly caused by prostate cancer (*Figure 1*).

Prostate cancer remained the leading cancer in males in the US from 1975–2016, and its incidence rate (per 100,000 population) rose from 94.0 in 1975 to a maximal peak of 237.5 in 1992, followed by a decline to 108.4 in 2016 (*Figure 2A*). The rapid uptake of prostate-specific antigen screening led to a dramatic spike in overall prostate cancer diagnoses during the early 1990s (7). Meanwhile, breast cancer remained the primary cancer in females in the US from 1975–2016, and showed an increased incidence rate (per 100,000 population) from 105.1 in 1975 to a maximal peak of 141.6 in 1999, followed by a subsequent drop to 126.5 in 2016 (*Figure 2B*). The breast cancer incidence rate in females reduced by 10.7% from 1999–2016, likely due to the decreased use of menopausal hormones (8,9). The decrease in incidence may also reflect (in part) the small declines in mammography screening since 2000 (9).

Lung and bronchial cancer remained the second major malignancy in males from 1975–2016, and in females from 1992–2016 (*Figure 2*). In males, the incidence of lung and bronchial cancer has exhibited a continuously declining trend since the 1980s (*Figure 2*), which reflects changes in risk behaviours following the promulgation of information about the dangers of tobacco smoking in the 1950s and 1960s, as well as subsequent governmental tobacco control measures (10). However, in females, the incidence of lung and bronchial cancer showed an increasing trend from

Incidenci rank	e Cancer		Five-year relati (959	ive survival rate % Cl)			ž	Ö	
[2016]		All races	White	All races	White	All races	White	All races	White
Male									
	All malignant cancers	68.5% (68.2–68.7%)	69.3% (69.1–69.6%)	65.6% (64.9–66.2%)	58.5% (57.8–59.2%)	404,243	318,681	44,713	34,724
-	Prostate	98.4%* (98.2*–98.7%*)	98.8%*(98.5*–99.0%*)	96.2%* (95.3*–96.9%*)	94.0% (92.7–95.1%)	116,247	87,951	17,745	7,776
2	Lung and bronchus	17.4% (16.9–18.0%)	17.6% (17.0–18.1%)	15.7% (14.2–17.2%)	17.9% (16.2–19.6%)	44,679	34,733	5,207	4,587
ю	Colon and rectum	66.0% (65.2–66.7%)	66.8% (65.8%–67.6%)	58.4% (56.1%–60.7%)	65.5%* (63.5*-67.5%*)	35,887	26,882	4,064	4,581
4	Urinary bladder	79.0% (78.0–80.0%)	79.5% (78.5–80.6%)	68.5% (63.9–72.7%)	73.6%* (69.6*–77.2%*)	24,674	21,781	1,200	1,401
2	Melanoma of the skin	92.7% (91.8–93.5%)	92.5% (91.6–93.3%)	65.4%* (44.6*–80.0%*)	67.2% <sup>#</sup> (56.7 <sup>#</sup> -75.7% <sup>#</sup> )	21,934	20,853	61	243
9	Lymphoma	76.1% (75.3–77.0%)	76.9% (75.9–77.9%)	71.5%* (68.8*–74.0%*)	69.9% <sup>#</sup> (67.0 <sup>#</sup> -72.5% <sup>#</sup> )	22,197	17,799	2,055	2,023
7	Kidney and renal pelvis	74.6% (73.5–75.6%)	74.3% (73.1–75.5%)	77.7% (74.8–80.4%)	69.7% (66.1–73.1%)	16,941	13,350	1,973	1,447
œ	Leukaemia	67.6% (66.4–68.7%)	68.3% (67.0–69.6%)	62.0% (57.5–66.2%)	56.9%# (53.0*-60.5%#)	13,558	11,211	1,030	1,064
6	Pancreas	10.5% (9.7–11.3%)	10.6% (9.7–11.5%)	9.3%* (7.0*–12.0%*)	9.6%* (7.2*–12.4%*)	11,392	8,915	1,287	1,145
10	Liver	21.2% (20.1–22.3%)	20.6% (19.3–21.9%)	17.0%# (14.4#–19.8%#)	26.2% (23.6–28.8%)	11,439	7,423	1,785	2,163
11	Myeloma	54.9% (53.0–56.8%)	54.4% (52.2–56.7%)	55.0%* (50.4*–59.4%*)	54.2% <sup>#</sup> (47.6 <sup>#</sup> -60.4% <sup>#</sup> )	6,800	4,947	1,209	581
12	Stomach	29.8% (28.3–31.3%)	29.1% (27.4–30.9%)	25.3% (21.0–29.8%)	33.7%* (30.1*–37.3%*)	7,345	5,057	938	1,302
13	Thyroid	95.9%* (94.8*–96.8%*)	96.4%* (95.1*–97.3%*)	92.8%* (84.5*–96.7%*)	92.7%* (88.8*–95.2%*)	6,475	5,315	320	736
14	Brain and other nervous system	31.8% (30.4–33.2%)	30.6% (29.1%–32.2%)	36.7% (30.7–42.8%)	34.5%# (29.1*-40.0%*)	6,817	5,766	453	531
14	Oesophagus	20.8% (19.4–22.3%)	22.2% (20.6–23.9%)	9.8%* (6.4*–14.1%*)	13.4%* (9.1*–18.4%*)	6,119	5,221	446	426
16	Testis	96.7%* (95.9*–97.4%*)	97.0%* (96.1*–97.6%*)	92.0%* (86.0*–95.6%*)	94.3%* (90.8*–96.5%*)	5,838	5,079	190	450
17	Tongue	69.9% (67.8–71.8%)	71.4% (69.2–73.4%)	51.0% (42.5–58.8%)	64.0% <sup>#</sup> (55.9 <sup>#</sup> -71.1% <sup>#</sup> )	4,698	4,097	275	296
18	Larynx	62.2% (60.0–64.4%)	63.7% (61.1–66.2%)	52.7% (46.6–58.6%)	62.0% <sup>#</sup> (52.5 <sup>#</sup> -70.2% <sup>#</sup> )	4,264	3,360	618	248
19	Soft tissue including heart	67.3% (64.9–69.6%)	68.5% (65.7–71.2%)	62.1%* (54.9*–68.5%*)	59.8%# (52.6 <sup>#</sup> -66.2% <sup>#</sup> )	3,285	2,511	356	373
20	Tonsil	78.6%# (76.4#–80.6%#)	80.6%# (78.3#–82.7%#)	59.4%# (50.8#-67.0%#)	74.4%# (63.0 <sup>#</sup> -82.8% <sup>#</sup> )	3,319	2,860	288	154

Table 3 (continued)

Table 3 (	(continued)								
Incidenc rank	e Cancer		Five-year rela (95	tive survival rate % Cl)			No	Ċ	
[2016]		All races	White	All races	White	All races	White	All races	White
Female									
	All malignant cancers	70.1% (69.9–70.3%)	71.2% (70.9–71.4%)	61.3% (60.7–62.0%)	69.3% (68.7–69.9%)	395,331	307,195	42,621	41,572
-	Breast	91.2% (90.9–91.6%)	92.3% (92.0–92.7%)	83.1% (82.1–84.1%)	91.4% (90.5–92.1%)	124,503	95,541	13,892	14,193
N	Lung and bronchus	24.6% (24.0–25.2%)	24.4% (23.8–25.1%)	23.5% (21.8–25.2%)	26.7% (24.7–28.7%)	41,772	33,182	4,766	3,705
e	Colon and rectum	66.2% (65.4–67.0%)	66.8% (65.8–67.7%)	59.9% (57.6–62.1%)	67.1% (64.9–69.2%)	32,815	24,431	4,209	3,855
4	Corpus and uterus	82.7% (82.0–83.4%)	85.5% (84.7–86.2%)	63.2% (60.7–65.6%)	81.2%* (79.2*–83.0%*)	29,573	22,801	3,160	3,353
5	Thyroid	99.0%* (98.8*–99.2%*)	99.2%* (99.0*–99.4%*)	97.4% (95.0–98.6%)	97.6%* (96.5*–98.4%*)	20,919	16,178	1,623	2,764
9	Melanoma of the skin	96.5% (95.8–97.1%)	96.5% (95.7–97.1%)	69.2% <sup>#</sup> (50.1 <sup>#</sup> -82.2% <sup>#</sup> )	81.8%* (72.5*–88.2%*)	17,595	16,597	84	233
7	Lymphoma	77.6% (76.7–78.5%)	78.4% (77.3–79.4%)	76.4% (73.3–79.2%)	69.4% (66.2–72.3%)	17,620	14,033	1,693	1,664
ω	Pancreas	9.5% (8.7–10.4%)	9.4% (8.5–10.4%)	9.4%* (7.4%*–11.7%*)	10.0% (7.7–12.7%)	11,169	8,404	1,511	1,226
6	Leukaemia	64.4% (63.0–65.7%)	65.3% (63.8–66.8%)	58.6% (53.9–62.9%)	53.3% (48.7–57.7%)	9,712	7,852	914	788
0	Kidney and renal pelvis	76.6% (75.3–77.9%)	76.3% (74.8–77.8%)	77.7%* (74.1*–80.9%*)	74.7%* (70.4*–78.5%*)	9,596	7,374	1,245	861
11	Ovary	48.9% (47.6–50.1%)	48.5% (47.1–49.9%)	42.7% (38.4–46.9%)	55.8% (51.7–59.6%)	11,881	9,462	1,088	1,258
12	Urinary bladder	75.2% (73.6–76.8%)	76.9%* (75.2*–78.5%*)	56.2% (50.1–61.8%)	69.8%* (63.6*–75.2%*)	7,730	6,504	623	494
13	Cervix uteri	69.6% (68.0–71.0%)	71.6% (69.8–73.3%)	56.7% (52.2–61.1%)	69.6%* (65.4*–73.4%*)	6,576	4,706	606	870
14	Myeloma	53.0% (50.9–55.0%)	52.3% (49.7–54.8%)	54.8% (50.3–59.0%)	49.3%* (42.0*–56.3%*)	5,511	3,697	1,269	502
15	Stomach	35.8% (34.0–37.7%)	35.5% (33.1–37.8%)	41.1% (36.3–45.9%)	31.8%* (28.0*–35.7%*)	4,699	2,892	756	1,006
15	Brain and other nervous system	35.2% (33.5–36.9%)	33.7% (32.0–35.5%)	41.0% <sup>#</sup> (34.8 <sup>#</sup> -47.0% <sup>#</sup> )	40.2% <sup>#</sup> (33.7 <sup>#</sup> -46.6% <sup>#</sup> )	5,252	4,399	398	398
17	Liver	23.3% (21.4–25.4%)	22.4% (19.9–25.0%)	18.0%* (13.6*–22.9%*)	28.9% (24.5–33.4%)	3,542	2,117	559	842
18	Soft tissue including heart	67.0% (64.2–69.6%)	67.8% (64.5–70.8%)	66.9%# (59.5#–73.2%#)	60.8% <sup>#</sup> (52.4 <sup>#</sup> –68.2% <sup>#</sup> )	2,522	1,839	358	294
19	Vulva	70.9% (67.6–74.0%)	71.0% (67.4–74.2%)	67.6% <sup>#</sup> (54.5% <sup>#</sup> –77.7% <sup>#</sup> )	69.8% (53.7–81.2%)	2,088	1,791	163	113
20	Tongue	69.1% (65.7–72.2%)	70.4% (66.6–73.8%)	43.1%* (29.7*–55.7%*)	70.2% (58.4–79.2%)	1,714	1,363	106	225
20	Small intestine	69.2% (66.0–72.2%)	71.5% (67.8–74.9%)	66.9%* (59.0*–73.6%*)	47.4% (33.1–60.4%)	1,956	1,432	357	146
<sup>#</sup> , the rel Asian/Pa	ative cumulative survival cific Islander. Rank is bas	increased from a prior in ed on age-adjusted cano	nterval and has been ad cer incidence rate in 201	justed. Other denotes oth 6. Cl, confidence interval.	ler races and ethnicities, i	ncluding A	merican I	ndian/AK	Native,

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1975–2005, and slightly decreased after 2005 (*Figure 2*). Varying historical patterns in tobacco uptake and cessation, as well as upturns in the prevalence of female smoking in some birth cohorts account for the different trends between males and females (2,11).

Colon and rectal cancer were the third most common cancer in males from 1975–2016, and similarly, in females from 1992–2016 (*Figure 2*). The incidence patterns for colon and rectal cancer are generally similar in men and women and have continued to decline from 1985–2016 in both sexes (*Figure 2*). Some researchers have attributed the long-term decline to changes in risk factors (e.g., decreased smoking and red meat consumption, and increased use of aspirin), as well as the introduction and dissemination of screening tests (12,13). Colonoscopy procedures, which are the predominant screening tests, tripled among adults aged  $\geq$ 50 years in the US, from 21% in 2000 to 60% in 2015 (2).

The overall cancer mortality rates in both males and females have continuously declined since the 1990s, falling by 33.6% in males from 1990-2016, and by 23.6% in females from 1991-2016 (Figure 1). This declining trend continues to date. The decrease in cancer mortality over the past three decades is primarily attributable to reductions in overall cancer incidence, advances in early detection, and improvements in treatment (1-3). Consistent with cancer incidence, from 1975–2016, the top three leading causes of cancer mortality were still lung and bronchial, prostate (men only), breast (women only), and colon and rectal cancers (Figure 3). The mortality rates for these cancers have continued to decline since approximately 1990, except for female lung cancer, which has declined since 2002. Specifically, the mortality of lung and bronchial cancer decreased by 48.2% in males from 1990-2016, and by 23.3% in females from 2002–2016 (Figure 3).

Furthermore, prostate cancer mortality in males fell by 50.6% from 1991–2016. Breast cancer mortality in females also declined by 39.8% from 1988–2016 (*Figure 3*). Moreover, colon and rectal cancer mortality decreased by 51.6% in males from 1978–2016, and in females by 54.7% from 1976–2016 (*Figure 3*). Some researchers have attributed the decline in mortality of these cancers to steady reductions in smoking and advances in early detection and treatment (11,13-16). Thus, it is important that efforts in tobacco control and smoking cessation continue so that further reductions in cancer incidence and mortality can be achieved, especially among women.

In terms of the cancer survival rate, the 5-year relative

survival rates for all cancers combined diagnosed from 2010-2016 were 68.5% in males and 70.1% in females (Table 3). Among the 10 leading cancers in 2016, those with a 5-year relative survival rate of less than 50% included lung and bronchial (17.4%), pancreatic (10.5%) and liver (21.2%) cancers in males, and lung and bronchial (24.6%) and pancreatic (9.5%) cancers in females (Table 3). The 5-year relative survival rate of these cancer types is low, partly because more than 50% of cases are diagnosed at a late stage (2). Due to early screening and treatment, the 5-year survival rates of prostate cancer and breast cancer are high (7,17-20), reaching 98.4% and 91.2%, respectively (Table 3). Greater attention should be given to cancers with a low survival rate, and knowledge and experience from the screening and treatment of prostate and breast cancers should be applied in order to strengthen early detection and treatment and prolong the survival time of patients with these types of cancer. Such issues are especially important for lung and bronchial cancer. Despite being the second most common cancer among both males and females in 2016, it was the leading cause of cancer death, primarily because the 5-year relative survival rate is extremely low (17.4% in males and 24.6% in females). There is a potential for earlier lung cancer diagnosis through screening with low-dose computed tomography (CT), which could significantly reduce lung cancer mortality (2,21-23). From 2010-2015, the percentage of eligible smokers who were reported to have undergone low-dose CT screening in the previous 12 months remained low and constant (3.3% in 2010 and 3.9% in 2015) (24). Therefore, the broad implementation of guideline-recommended lung cancer screening needs to be strengthened in the future to benefit more people.

In addition, there are noticeable differences in cancer incidence, mortality, and survival rates among sex and ethnicity categories. From 1975–2016, overall cancer incidence and mortality was higher in males than females (*Figure 1*). Biological, behavioural, and environmental factors all contribute the higher cancer incidence and mortality rates of men compared to women (25). Dunford *et al.* reported that biallelic expression of "escape from X-inactivation tumour-suppressor" genes in females explains a portion of the reduced cancer incidence in females as compared with males across a variety of tumour types (26). Also, black males have higher incidence and mortality, and shorter survival rates compared with white males for all cancers combined. However, black females have a lower incidence, higher mortality, and shorter

survival rates relative to white females for all cancers combined. In the US, black people are more likely to report not being able to see a doctor because of cost (27). In addition, they have notably lower educational attainment and homeownership, as well as approximately twice the proportion of households living below the poverty line and approximately twice the levels of unemployment compared to the white population (27). These socio-economic factors help to explain ethnic disparities in cancer incidence, mortality, and survival rates via cancer-related behaviours and health care utilisation, which constrain an individual's ability to engage in cancer prevention, early detection, or treatment (28). Finally, it is unsurprising that there are different high-incidence cancers among the different age groups. Cancer screening and prevention should focus on the high-incidence cancers of these different age groups.

# Limitations

A strength of our study is the use of nationwide, highquality, population-based data on cancer incidence, mortality and survival rates from the SEER database. However, our study has several limitations that should be noted. Firstly, due to the descriptive nature of this study, it is only possible to speculate about potential explanations for cancer incidence and mortality trends. Secondly, the rapid uptake of cancer screening led to a dramatic increase in the incidence of certain cancers, such as prostate cancer, and this increase in incidence does not necessarily reflect the actual change in cancer incidence. However, mortality, which we also analysed, is less affected by screening and can offer an accurate reflection the actual situation. Thirdly, the SEER database only contains data on patients within US regions and does not represent changes in the incidence, mortality, and survival rates of cancer worldwide. We anticipate the establishment of a record similar to the SEER database in China, which will represent a population of 1.4 billion.

## Conclusions

The continuous decline in the overall cancer mortality rate in the US since the early 1990s has resulted in an overall decrease of 33.6% among males and 23.6% among females. The top three leading cancers and causes of cancer death in males from 1975–2016 were prostate, lung and bronchial, and colon and rectal cancers, while in females (from 1979–2016), they were breast, lung and bronchial, and colon and rectal cancers. The 5-year relative survival rates for all cancers combined (diagnosed from 2010–2016) were 68.5% in males and 70.1% in females. From 1975–2016, the overall cancer incidence and mortality were higher in males than females. Black males have a higher incidence and mortality, and shorter survival rates compared with white males for all cancers combined. However, black females have a lower incidence, higher mortality, and shorter survival rates compared with white females for all cancers combined. Our work provides a comprehensive overview of cancer incidence and mortality in the US over the past 42 years. More research is needed to elucidate the causes of change in cancer incidence and mortality, and advance early detection and treatment of cancers with a low survival rate.

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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