Recent Time Trends in the Epidemiology of Stage IV Prostate Cancer in the United States: Analysis of Data From the Surveillance, Epidemiology, and End Results Program*

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Abstract

OBJECTIVES—To describe recent epidemiologic trends in stage IV prostate cancer. Although advances in screening and diagnostic techniques have led to earlier detection of prostate cancer, a portion of patients still present with late-stage disease.

METHODS—Population-based cancer registry data from the Surveillance, Epidemiology, and End Results Program (cases from 1988 to 2003, follow-up through 2005) were used to calculate annual age-adjusted incidence rates of stage IV prostate cancer (overall and for the subset presenting with distant metastases) and to assess time trends in patient, tumor, and treatment characteristics and survival.

RESULTS—From 1988 to 2003, the age-adjusted incidence of stage IV prostate cancer significantly declined by 6.4% each year. The proportion of men diagnosed at younger ages, with poorly differentiated tumors, or who underwent a radical prostatectomy significantly increased over time. Five-year relative survival improved across the study period (from 41.6% to 62.3%), particularly in those diagnosed at younger ages or with moderately to well-differentiated tumors. Later years of diagnosis were independently associated with a decreased risk of death (from all causes and from prostate cancer specifically) after controlling for important patient, tumor, and treatment characteristics. Tumor grade and receipt of radical prostatectomy appeared to be the strongest independent prognostic indicators. Temporal trends were similar in the subset presenting with distant metastases, except that no significant improvement in survival was observed.

CONCLUSIONS—As younger men may expect to live longer with advanced prostate cancer, there remains a need to widen the range of therapeutic and supportive care options.

Prostate cancer is the most common invasive cancer diagnosed among men in the United States and is the second leading cause of cancer death, with an expected 192 280 new patients and 27 360 deaths in 2009.[1] Although the development and widespread use of the

prostate-specific antigen screening test for early prostate cancer detection in the late 1980s led to an approximate 2-fold increase in the incidence of the disease, the American Cancer Society has reported a 2.7% average annual decline in prostate cancer death rates since 1993.[2] A downward shift in clinical and pathologic stage has also been observed, with the greatest proportion of prostate cancer patients being diagnosed with organ-confined disease;[3–5] but this trend appears to have diminished in recent years.[6]

Despite the apparent stage migration and improvement in long-term survival, however, an estimated 4% of prostate cancer patients currently present with metastatic disease at the time of diagnosis.[7] For these individuals, successfully managing the disease still poses a significant challenge and the prognosis is discouraging. Although several studies have previously reported on trends in prostate cancer epidemiology,[8–13] limited data exist on recent temporal changes in those diagnosed specifically with advanced disease specifically. To better understand the changing characteristics and prognosis in this subset of patients, we examined recent time trends in the epidemiology of newly diagnosed stage IV prostate cancer in the United States using data from the Surveillance, Epidemiology and End Results (SEER) Program.

MATERIAL AND METHODS

Data Source

We used data from the National Cancer Institute's SEER Program, an authoritative source of population-based information on cancer incidence and survival in the United States.[14] SEER registries routinely collect information on patient demographics; primary tumor site, morphology, and stage at diagnosis; first course of treatment; and follow-up for vital status. To assess epidemiologic trends over time and maximize years of coverage, we limited our analyses to the first 9 registries supported by SEER (Connecticut, Iowa, New Mexico, Utah, Hawaii, Atlanta, Detroit, San Francisco-Oakland, and Seattle–Puget Sound), which cover approximately 10% of the US population.

Study Population

For incidence estimates, we selected male patients with a primary diagnosis of stage IV (American Joint Committee on Cancer, 3rd ed. staging criteria) prostate cancer (C61.9, International Classification of Diseases for Oncology, 3rd ed.), diagnosed between January 1, 1988 and December 31, 2003 (n = 29 447 [100%]). For all remaining analyses, we limited our sample to include patients with a first and only primary diagnosis of stage IV prostate cancer (n = 24 657 [84%]). We excluded patients aged less than 35 years (n = 18 [<1%]), those who with unknown treatment status (n = 327 [1%]), and those that were identified by death certificate or autopsy only (n = 61 [<1%]). Given that the natural history of primary distant stage prostate cancer may be unique compared with the larger stage IV population, we also performed analyses separately on this subset.

Statistical Analysis

We calculated incidence rates by year of diagnosis (age-adjusted to the 2000 US standard population) and estimated the average annual percentage change in incidence by fitting a

least squares regression line to the natural logarithm of the incidence rates (with year of diagnosis as the regressor variable) using the National Cancer Institute's SEER/Stat software version 6.4.4 (Available at: http://www.seer.cancer.gov/seerstat).

We examined the distribution of incident stage IV prostate cancer patients by 3 approximately equivalent time periods of diagnosis (1988–1992, 1993–1997, and 1998–2003) according to age, ethnicity/race, tumor grade, and receipt of surgery and radiation as part of first-line therapy (ie, treatment within 4 months after diagnosis). Surgery was categorized according to receipt of cancer-directed surgery; radical/total prostatectomy, other surgery (including local tumor destruction/excision and subtotal/simple prostatectomy), or none. Receipt of radiation was classified into external beam radiation, other (radioactive implants only, radioisotopes only, or radiation not otherwise specified), and none. Cochran–Armitage chi-square tests for trend[15,16] were used to describe changes in the proportion of patients according to these characteristics by time period of diagnosis. The statistical software Stata/SE 9.1 for Windows (StataCorp LP, College Station, Texas) was used for these analyses.

Data on vital status were available through December 31, 2005. To describe 5-year survival, we limited our analyses to patients diagnosed up through December 31, 2001 to ensure at least 5 years of follow-up for each patient. Using SEER/Stat, we estimated 5-year relative and observed survival rates through the actuarial method first by the year of diagnosis and then by select demographic, tumor, and treatment variables according to time period of diagnosis. To further evaluate the association between period of diagnosis and risk of death after adjusting for age, ethnicity/race, tumor grade, and cancer-directed treatment, we used Stata/SE 9.1 statistical software to build Cox proportional hazard models.[17] Patients were followed from the date of diagnosis (1988–2003) until the date of death and censored at the date last known to be alive (if lost to follow-up) or December 31, 2005, whichever came first. We separately examined overall and prostate cancer-specific survival. For the latter analysis, patients who died of nonprostate cancer causes were considered censored at their date of death. Because SEER reports survival time in months, patients who survived for less than 31 days were excluded from these analyses.

RESULTS

Incidence

The annual age-adjusted incidence of stage IV prostate cancer decreased from 28.1 per 100 000 (95% confidence interval [CI], 26.9–29.3) in 1988 to 12.3 per 100 000 (95% CI, 11.7–13.0) in 2003, representing an average 6.4% annual decline (95% CI, −7.8 to −4.9). For the subset with distant metastases at diagnosis, this downward trend was even steeper; age-adjusted incidence fell from 18.4 per 100 000 (95% CI, 17.4–19.4) in 1988 to 6.7 per 100 000 (95% CI, 6.3–7.3) in 2003, representing an average annual drop of 8.0% (95% CI, −9.3 to −6.7).

Patient, Tumor, and Treatment Characteristics

Patient, tumor, and treatment characteristics for stage IV prostate cancer patients diagnosed in the SEER 9 registries by time period of diagnosis as well as an assessment of trends in these characteristics over time are described in Table 1 for all stage IV patients (n = 24 251) and for the stage IV patients with distant metastases (n = 14 774). For all stage IV prostate cancer patients combined, the proportion of men diagnosed at younger ages increased significantly across the study period. Specifically, among men diagnosed during 1988–1992, just 1.0% were aged 35–50, 2.6% were aged 51–55, and 6.8% were aged 56–60 years. For those diagnosed in more recent years (1998–2003), these proportions increased to 4.4% (*P* <.0001), 8.5% (*P* <.0001), and 12.5% (*P* <.0001), respectively. For the distant stage subset, similar but less pronounced increases in proportions of younger men were evident, but there was also a rise in the proportion of those aged 81+ years.

The percentage of stage IV tumors that were poorly differentiated at diagnosis significantly increased across the study period, from 42.7% (1988–1992) to 48.8% (1998–2003) (*P* <. 0001), whereas the proportion of those of lower grades decreased. Trends were similar in the distant stage subset, although the decline in moderately differentiated tumors in this group was much greater (29.7% in 1988–1992 to 19.1% in 1998–2003, *P* <.0001). When temporal changes in tumor grade were examined by receipt of cancer-directed surgery, patterns were similar except that in surgically treated patients, the percentage of moderately differentiated tumors significantly increased in the overall stage IV group (with a less pronounced increase in the proportion of poorly differentiated tumors), whereas there was a steeper increase in the proportion of poorly differentiated tumors in the subset with distant metastases.

Over time, there was a significant increase in the proportion of stage IV prostate cancer patients electing a radical prostatectomy as first-line treatment, from 10.0% in 1988–1992 to 32.7% in 1998–2003 (*P* <.0001), and a concurrent sharp decline in those receiving other types of cancer-directed surgeries. However, for those with distant metastases at diagnosis, there was an upward shift in the percentage of men not receiving any type of cancer-directed surgery (67.4% [1988–1992] to 88.9% [1998–2003], *P* <.0001), and relatively few underwent radical prostatectomy during any period of diagnosis. Although there was a detectable increase in the proportion of stage IV patients who received radiation as part of first-line therapy, primarily in the distant stage subset, over 75% did not receive any form of radiation across the study period.

Survival

Five-year relative survival for stage IV prostate cancer patients increased from 41.6% for individuals diagnosed in 1988 to 62.3% for those diagnosed in 2001 (Fig. 1). However, for the distant stage subset, survival was 25.0% for patients diagnosed in 1988, peaked to 36.2% in 1992, and declined to 27.0% in 2001, resulting in very little net improvement in prognosis across the study period (Fig. 1). When survival was examined according to patient, tumor, and treatment characteristics by time period of diagnosis, estimates of 5-year relative survival increased among all stage IV patients except in those who were older than 70 years or had undergone cancer-directed surgery other than radical prostatectomy (Table 2). Improvements in survival were particularly dramatic for patients diagnosed with moderately

to well-differentiated tumors and for those diagnosed at younger ages, especially for those aged 35–60 years. Trends in survival over time were very different for the distant stage subset, remaining stable or decreasing in all groups except for those who were younger than 71 years or diagnosed with moderately to well-differentiated tumors (Table 2).

Mirroring these temporal trends in 5-year survival, results of Cox proportional hazard regression modeling indicated that after controlling for age, ethnicity/race, tumor grade, and receipt of cancer-directed treatments, there was a decreased risk of death (both from all causes and from prostate cancer specifically) over time for men diagnosed with stage IV prostate cancer (Table 3). Those diagnosed in either 1993–1997 or 1998–2003 had a 9% decreased risk of death from prostate cancer compared with those diagnosed in 1988–1992. For the subset presenting with distant metastases, however, there was no significant change in the risk of death across the study period. For all patients, tumor grade and receipt of radical prostatectomy appeared to be the strongest prognostic indicators.

COMMENT

Consistent with studies reporting downward time trends in rates of metastatic prostate cancer,[18,19] we observed a significant decline in the annual incidence of stage IV prostate cancer from 1988 to 2003. To our knowledge, the current study represents the only recent report focused on examining temporal trends in the distribution of patient, tumor, and treatment characteristics and survival for newly diagnosed stage IV prostate cancer. We observed significant changes in patient demographics across the study period, most notably with respect to age at diagnosis. Previous research has noted a shift toward younger ages at diagnosis for all stages of prostate cancer combined,[10,13] and we found that this same trend holds when stage IV tumors are examined separately. However, Barnholtz-Sloan et al[20] examined time trends in meta-static prostate cancer using data from the Detroit SEER registry (1973–1997), and they indicated a decrease in the percentage of men diagnosed at ages <60 years. Conversely, among our distant stage subset, the proportion of those aged 60 years or less rose from 8.5% (1988–1992) to over 15% (1998–2003). Discordance in these findings may be attributed to differences in time period and geographic coverage, as well as nuances in tumor inclusion criteria. Regardless, prostate cancer is still rare in younger men, particularly under the age of 50, and this group may therefore be less likely to suspect it, be screened for it, or have their doctor propose a diagnostic work-up when symptoms surface. Hence, it has been suggested that differential screening behavior may be causing younger men to account for a greater proportion of more advanced tumors in recent years.[21]

We also discovered an upward migration in stage IV prostate tumor grade at diagnosis, which is consistent with earlier reports on prostate cancer overall[22,23] and metastatic disease specifically.[10,20] Hankey et al[10] proposed that, in addition to a screening effect, shifts in the grade distribution among all prostate tumors may reflect changes in the use of available therapies. In the early 1980s, radical prostatectomy was modified to preserve regional innervation and potency, which led to an increase in the uptake of this procedure through the 1980s and into the 1990s. It is widely recognized that tumors are upgraded following surgery (because of the amount of tissue given to the pathologist for review), so an increase in radical prostatectomy procedures may have at least partly contributed to the shift in tumor

grade distribution toward higher grades. Indeed, we found a steep rise in the percentage of stage IV prostate cancer patients undergoing radical prostatectomy across the study period. However, in our subset of stage IV patients with distant metastases, although we observed relatively fewer moderately to well-differentiated tumors over time, only a small percentage underwent radical prostatectomy, and receipt of other types of cancer-directed surgeries declined considerably across the study period. Further, when temporal changes in tumor grade migration were examined separately for surgically versus nonsurgically treated patients, a shift toward higher tumor grades was consistently demonstrated across time for both groups.

It is well-documented that in recent years, survival has improved for men with prostate cancer in the United States.[8,10,12,20] Our study demonstrates that this is also true for patients diagnosed with stage IV disease. We observed an absolute increase of nearly 21% in 5-year relative survival across the study period, and later years of diagnosis were independently associated with improvements in survival after controlling for important patient, tumor, and treatment characteristics. Based on advances in screening and diagnostic techniques, it is likely that at least a portion of individuals are being diagnosed earlier in the disease process and are therefore surviving longer; but improvements may also be credited to increasingly successful treatment options for patients with advanced disease.[24] For the stage IV patients with distant metastases at diagnosis, however, rates of 5-year survival slightly increased only for younger men or for those with moderately to well-differentiated tumors, suggesting that only a subset of patients with distant stage prostate cancer has benefited from more aggressive or better systemic therapies. Further, no real improvement in prognosis for this group is yet evident, as multivariate analyses of survival revealed no significant change in the risk of all-cause or prostate cancer-specific death across the 3 time periods examined.

We also found that older age (71+ years), black ethnicity/race, higher tumor grade, and lack of radical prostatectomy generally conferred a poorer prognosis for stage IV patients, most likely reflecting differences between subgroups of patients with respect to biological factors related to survival, access to care, nature and extent of comorbidity, and response to available treatments. The prognostic role of age in prostate cancer, specifically, has been a subject of debate, and we detected a distinct pattern of disparate outcomes by age group for stage IV patients. Regardless of time period of diagnosis, 5-year relative survival increased, peaked, and then decreased with increasing age, and this trend was echoed in our adjusted age-specific death hazard ratios. Some research has demonstrated superior survival in younger patients, while other investigations have noted that younger men present with prostate cancer that is more aggressive, too advanced for radical surgery, and rapidly fatal.[21] Although we observed improvements in survival over time for men diagnosed at younger ages, our results also provide evidence that, at least for advanced prostate cancer, men diagnosed at either especially young (50 years) or old (71+ years) ages tend to have a poorer prognosis compared to the middle-aged group.

The SEER Program provides high-quality data on cancer incidence and survival in the United States, but any time trend investigation can be complicated by modifications in disease classification, advancements in diagnostic techniques, fluctuations in the popularity and availability of screening, and stage and grade migration. Our study was focused

exclusively on newly diagnosed prostate cancer patients classified as having stage IV disease consistent with the American Joint Committee on Cancer 3rd ed. staging criteria, and we performed separate analyses on the subset presenting with distant metastases in recognition of the heterogeneity of the stage IV group. We also attempted to limit the effect of tumors being upgraded because of surgery by describing time trends in tumor grade distribution separately for surgically versus nonsurgically treated patients and by combining moderately differentiated and well-differentiated tumors in our survival analyses. More generally, inherent to any population-based disease registry is the potential for inaccurate cause of death information (obtained from death certificates). Although the level of this type of attribution bias across SEER data are unknown, Penson et al[25] reported that for prostate cancer patients from the Seattle-Puget Sound SEER Registry, there was excellent agreement (97%) between clinician-assigned cause of death (based on medical chart review) and the cause of death on the death certificate (kappa = 0.91). Further, trained nosologists code cause of death information on death certificates, which are based on standardized procedures developed by the National Center for Health Statistics and are routinely reviewed for quality. It seems reasonable to assume that any potential discrepancies in the coding of cause of death would be consistent across time, geographic regions, and population groups in the United States. We chose to examine relative survival, prostate cancer-specific mortality, and overall mortality, and all 3 of these approaches yielded consistent findings. Unfortunately, we were unable to evaluate additional factors of interest in prostate cancer, such as prostate-specific antigen levels, Karnofsky performance status, site of metastases, and differences in other important therapies (eg, androgen deprivation therapy) over the study period, because these data are either incomplete or unavailable in SEER.

CONCLUSIONS

This descriptive study on recent time trends in the epidemiology of stage IV prostate cancer in the United States has important clinical implications. Perhaps one of the most striking findings is that younger men are representing an increasingly higher proportion of stage IV prostate tumors, and survival in this group is improving. As younger men may expect to live longer with advanced disease, long-term management of their condition must be carefully planned, particularly with respect to quality of life. For stage IV patients who present with distant metastases, our findings suggest no significant change in overall or prostate cancer-specific survival and only modest improvements in 5-year relative survival for those who are younger or have moderately to well-differentiated tumors, further highlighting the need for a wider range of supportive care and therapeutic options available to treat late-stage disease.

Acknowledgments

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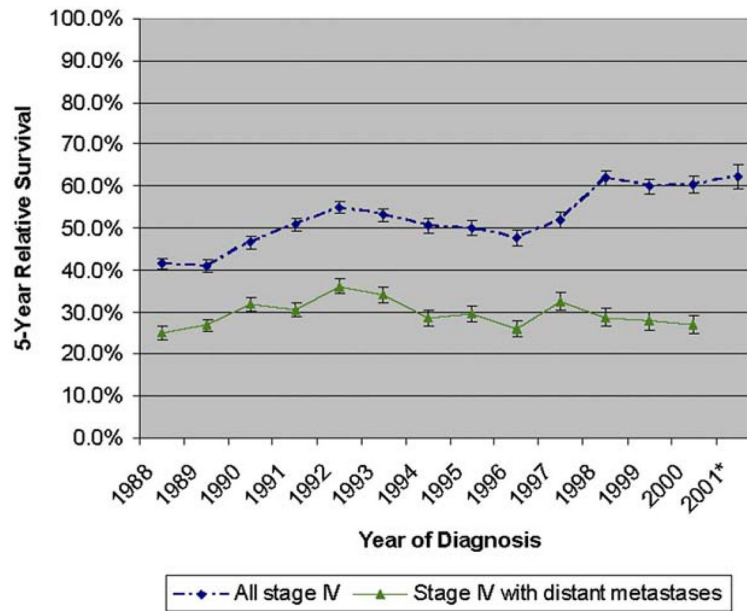
Figure 1.
Time trend in 5-year relative survival (%) for all stage IV prostate cancer patients and for those with distant metastases at diagnosis by year of diagnosis with follow-up through 2005. *indicates unable to calculate for those diagnosed with distant metastases in the year 2001 based on too few patients and insufficient follow-up time.

Table 1

Distribution of stage IV prostate cancer patients according to select variables by time period of diagnosis in the SEER 9 registries

Characteristics*	Period of Diagnosis			Overall Trend†	
	1988–1992	1993–1997	1998–2003	+/−	P
All Stage IV	(n = 10 026)	(n = 6454)	(n = 7771)		
Age					
35–50 y	1.0%	2.9%	4.4%	+	<.0001
51–55 y	2.6%	4.4%	8.5%	+	<.0001
56–60 y	6.8%	8.1%	12.5%	+	<.0001
61–65 y	13.7%	14.5%	15.3%	+	.0020
66–70 y	20.3%	18.3%	16.0%	−	<.0001
71–75 y	21.2%	18.5%	14.6%	−	<.0001
76–80 y	16.3%	14.4%	12.1%	−	<.0001
81+ y	18.2%	19.1%	16.5%	−	.0095
Mean (SD), years	71.9 (9.1)	70.9 (10.3)	68.7 (11.1)		
Ethnicity/race					
White	80.2%	77.4%	77.8%	−	.0001
Black	14.2%	15.2%	14.4%	+	.6822
Other/unknown	5.6%	7.4%	7.8%	+	<.0001
Tumor grade					
Surgically treated patients					
Well-differentiated	5.2%	2.8%	0.5%	−	<.0001
Moderately differentiated	36.2%	41.1%	45.4%	+	<.0001
Poorly differentiated	48.8%	49.3%	51.4%	+	.0274
Undifferentiated	2.9%	1.9%	1.0%	−	<.0001
Unknown	6.9%	4.9%	1.8%	−	<.0001
Nonsurgically treated patients					
Well-differentiated	4.6%	2.4%	0.6%	−	<.0001
Moderately differentiated	31.2%	28.7%	22.4%	−	<.0001
Poorly differentiated	37.5%	40.8%	46.9%	+	<.0001
Undifferentiated	2.1%	1.5%	1.3%	−	.0012

Characteristics*	Period of Diagnosis			Overall Trend†	
	1988–1992	1993–1997	1998–2003	+/−	P
All Stage IV	(n = 10 026)	(n = 6454)	(n = 7771)		
Unknown	24.6%	26.7%	28.7%	+	<.0001
Overall					
Well-differentiated	4.9%	2.5%	0.6%	−	<.0001
Moderately differentiated	33.5%	33.3%	31.9%	−	.0297
Poorly differentiated	42.7%	44.0%	48.8%	+	<.0001
Undifferentiated	2.5%	1.7%	1.2%	−	<.0001
Unknown	16.4%	18.6%	17.6%	+	.0276
Cancer-directed surgery					
None	54.1%	62.6%	58.7%	+	<.0001
Radical/total prostatectomy	10.0%	13.9%	32.7%	+	<.0001
Other cancer-directed surgery	36.0%	23.5%	8.6%	−	<.0001
Radiation					
None	78.4%	80.3%	76.5%	−	.0040
Beam radiation	21.2%	19.3%	22.7%	+	.0422
Other radiation	0.4%	0.5%	0.9%	+	<.0001
Stage IV with distant metastases	(n = 6 542)	(n = 4 193)	(n = 4 039)		
Age					
35–50 y	0.9%	2.2%	3.0%	+	<.0001
51–55 y	2.0%	2.8%	4.9%	+	<.0001
56–60 y	5.6%	5.8%	7.5%	+	.0002
61–65 y	11.3%	10.9%	9.7%	−	.0085
66–70 y	17.6%	15.9%	13.3%	−	<.0001
71–75 y	20.5%	19.7%	17.0%	−	<.0001
76–80 y	19.1%	17.9%	17.6%	−	.0417
81+ y	23.0%	24.9%	27.2%	+	<.0001
Mean (SD), years	73.4 (9.2)	73.2 (10.1)	72.9 (11.0)		
Ethnicity/race					
White	78.3%	76.0%	75.0%	−	.0001
Black	16.9%	16.2%	16.2%	−	.3132

Characteristics*	Period of Diagnosis			Overall Trend†	
	1988–1992	1993–1997	1998–2003	+/−	P
	(n = 10 026)	(n = 6454)	(n = 7771)		
All Stage IV					
Other/unknown	4.8%	7.8%	8.8%	+	<0.0001
Tumor grade					
Surgically treated patients					
Well-differentiated	5.5%	2.1%	0.5%	−	<.0001
Moderately differentiated	28.6%	27.5%	18.0%	−	<.0001
Poorly differentiated	53.9%	60.2%	72.6%	+	<.0001
Undifferentiated	3.6%	2.5%	2.5%	−	.1053
Unknown	8.4%	7.7%	6.5%	−	.1493
Nonsurgically treated patients					
Well-differentiated	4.1%	2.2%	0.5%	−	<.0001
Moderately differentiated	30.3%	26.9%	19.3%	−	<.0001
Poorly differentiated	36.4%	40.0%	45.5%	+	<.0001
Undifferentiated	2.2%	1.3%	1.2%	−	.0002
Unknown	27.0%	29.6%	33.6%	+	<.0001
Overall					
Well-differentiated	4.6%	2.2%	0.5%	−	<.0001
Moderately differentiated	29.7%	27.1%	19.1%	−	<.0001
Poorly differentiated	42.1%	43.9%	48.5%	+	<.0001
Undifferentiated	2.6%	1.6%	1.3%	−	<.0001
Unknown	21.0%	25.4%	30.6%	+	<.0001
Cancer-directed surgery					
None	67.4%	80.8%	88.9%	+	<.0001
Radical/total prostatectomy	0.9%	1.2%	0.8%	−	.6554
Other cancer-directed surgery	31.7%	18.0%	10.3%	−	<.0001
Radiation					
None	83.6%	82.7%	78.3%	−	<.0001
Beam radiation	16.2%	16.7%	20.7%	+	<.0001
Other radiation	0.2%	0.6%	1.0%	+	<.0001

SD indicates standard deviation; SEER, Surveillance, Epidemiology, and End Results.

*
Percentages may not add up to 100 due to rounding.

†
Based on Cochran–Armitage chi-squares tests for trends in proportions by time period of diagnosis.

Table 2

Five-year observed and relative survival for stage IV prostate cancer patients according to select variables by time period of diagnosis based on data from the SEER 9 registries[*]

Characteristics	Period of Diagnosis					
	1988–1992		1993–1997		1998–2001	
	Observed	Relative	Observed	Relative	Observed	Relative
	(n = 10 026)		(n = 6 450)		(n = 5 192)	
	5-Year Survival (SE)					
All stage IV						
Age						
35–50 y	32.0% (4.7)	33.0% (4.8)[†]	49.6% (3.7)	51.0% (3.8)[†]	62.9% (3.3)	64.8% (3.4)[†]
51–60 y	46.0% (1.6)	49.8% (1.8)	55.8% (1.8)	59.6% (1.9)	72.2% (1.4)	76.7% (1.5)
61–70 y	42.9% (0.8)	50.5% (1.0)	50.0% (1.1)	57.6% (1.3)	63.1% (1.2)	72.0% (1.4)
71+ y	27.6% (0.6)	44.1% (1.0)	26.7% (0.8)	42.0% (1.2)	26.4% (0.9)	41.1% (1.5)
Ethnicity/race						
White	35.9% (0.5)	49.0% (0.7)	38.9% (0.7)	51.2% (0.9)	49.5% (0.8)	62.8% (1.0)
Black	26.3% (1.2)	36.8% (1.6)	32.7% (1.5)	44.2% (2.0)	41.7% (1.8)	53.5% (2.4)[†]
Other/unknown	36.2% (2.0)	46.4% (2.6)	48.2% (2.3)	59.7% (2.9)	50.8% (2.5)	61.8% (3.0)
Tumor grade						
Well-/moderately differentiated	46.8% (0.8)	62.2% (1.1)	56.1% (1.0)	70.5% (1.3)	74.1% (1.0)	88.2% (1.2)
Poorly/undifferentiated	29.7% (0.7)	40.1% (0.9)	34.0% (0.9)	43.9% (1.1)	43.0% (1.0)	53.7% (1.3)
Unknown	19.5% (1.0)	29.1% (1.5)	16.2% (1.1)	24.5% (1.6)	11.2% (1.1)	17.1% (1.6)
Cancer-directed surgery						
None	24.7% (0.6)	34.7% (0.8)	26.9% (0.7)	36.9% (1.0)	29.5% (0.8)	39.7% (1.1)
Radical/total prostatectomy	83.0% (1.2)	98.7% (1.4)	88.6% (1.1)	99.8% (1.2)[†‡]	91.3% (0.7)	100.0% (0.2)[†‡]
Other cancer-directed surgery	36.0% (0.8)	49.1% (1.1)	40.4% (1.3)	52.4% (1.6)	28.1% (2.1)	39.4% (3.0)
Beam radiation						
No	32.1% (0.5)	44.6% (0.7)	37.4% (0.7)	49.9% (0.9)	47.1% (0.8)	60.6% (1.0)
Yes	43.8% (1.1)	55.9% (1.4)	43.9% (1.4)	54.6% (1.8)	53.4% (1.5)	64.1% (1.8)
Overall	34.6% (0.5)	47.2% (0.6)	38.6% (0.6)	50.8% (0.8)	48.5% (0.7)	61.5% (0.9)
Stage IV with distant metastases at diagnosis	(n = 6 542)		(n = 4 191)		(n = 2 719)	
Age						

Characteristics	Period of Diagnosis					
	1988–1992		1993–1997		1998–2001	
	5-Year Survival (SE)					
	Observed	Relative	Observed	Relative	Observed	Relative
	(n = 10 026)		(n = 6 450)		(n = 5 192)	
All stage IV						
35–50 y	13.6% (4.5)	14.0% (4.6)[†]	23.3% (4.5)	24.0% (4.6)[†]	21.5% (4.7)	22.2% (4.8)[†]
51–60 y	23.4% (1.9)	25.4% (2.1)	24.7% (2.3)	26.4% (2.4)	27.9% (2.7)	29.7% (2.9)
61–70 y	24.2% (1.0)	28.7% (1.2)	26.6% (1.3)	30.7% (1.5)	30.7% (1.9)	35.3% (2.1)
71+ y	19.5% (0.6)	32.0% (1.0)	19.5% (0.8)	31.2% (1.2)	15.5% (0.9)	24.9% (1.5)
Ethnicity/race						
White	21.3% (0.6)	30.4% (0.8)	21.4% (0.7)	29.8% (1.0)	20.0% (0.9)	28.0% (1.3)
Black	18.2% (1.2)	26.0% (1.7)	17.9% (1.5)	25.0% (2.1)	18.8% (1.9)	25.5% (2.6)
Other/unknown	28.4% (2.6)	37.6% (3.4)	35.3% (2.7)	44.9% (3.4)	29.1% (3.0)	36.9% (3.8)
Tumor grade						
Well-/moderately differentiated	29.9% (1.0)	41.6% (1.3)	34.5% (1.4)	46.1% (1.8)	42.8% (2.1)	56.2% (2.7)
Poorly/undifferentiated	17.2% (0.7)	24.1% (1.0)	19.4% (0.9)	25.9% (1.2)	18.0% (1.1)	23.7% (1.5)
Unknown	14.9% (1.0)	22.8% (1.5)	11.9% (1.0)	18.4% (1.5)	8.4% (1.0)	12.9% (1.5)
Cancer-directed surgery						
None	20.5% (0.6)	29.1% (0.9)	21.8% (0.7)	30.3% (1.0)	20.6% (0.8)	28.4% (1.2)
Radical/total prostatectomy	72.1% (5.7)	86.4% (6.9)[‡]	76.9% (5.8)	86.6% (6.2)[‡]	68.9% (10.9)	80.9% (12.8)
Other cancer-directed surgery	21.0% (0.9)	30.0% (1.3)	18.8% (1.4)	25.6% (1.9)	17.3% (2.3)	24.1% (3.2)
Beam radiation						
No	21.1% (0.6)	30.3% (0.8)	22.2% (0.7)	31.0% (1.0)	20.7% (0.9)	29.0% (1.3)
Yes	21.2% (1.3)	28.3% (1.7)	20.6% (1.5)	26.9% (2.0)	20.4% (1.8)	26.3% (2.3)
Overall	21.1% (0.5)	30.0% (0.7)	21.9% (0.6)	30.3% (0.9)	20.6% (0.8)	28.4% (1.1)

SE indicates standard error.

[*] Survival calculated based on actuarial method.

[†] The relative cumulative rate increased from a prior interval and has been adjusted.

[‡] The relative cumulative rate is over 100% and has been adjusted.

Table 3

Multivariate regression analysis of factors associated with time to death (overall and prostate cancer-specific) based on the Cox proportional hazards model for males diagnosed with stage IV prostate cancer who survived at least 31 days based on data from the SEER 9 registries

Characteristics	All Causes of Death			Prostate Cancer-Specific Death		
	aHR*	95% CI	P	aHR*	95% CI	P
All stage IV (n = 23 845)						
Time of diagnosis						
1988–1992	1.00	Reference		1.00	Reference	
1993–1997	0.92	0.89–0.95	<.001	0.91	0.87–0.95	<.001
1998–2003	0.90	0.86–0.93	<.001	0.91	0.87–0.95	<.001
Age						
35–50 y	0.68	0.61–0.76	<.001	0.98	0.87–1.10	.744
51–60 y	0.62	0.59–0.65	<.001	0.82	0.78–0.87	<.001
61–70 y	0.70	0.68–0.73	<.001	0.85	0.81–0.88	<.001
71+ y	1.00	Reference		1.00	Reference	
Ethnicity/race						
White	1.00	Reference		1.00	Reference	
Black	1.16	1.12–1.21	<.001	1.11	1.06–1.17	<.001
Other/unknown	0.74	0.69–0.78	<.001	0.68	0.63–0.74	<.001
Tumor grade						
Well-/moderately differentiated	1.00	Reference		1.00	Reference	
Poorly/undifferentiated	1.62	1.56–1.68	<.001	1.87	1.80–1.96	<.001
Unknown	2.07	1.98–2.16	<.001	2.32	2.20–2.44	<.001
Cancer-directed surgery						
None	1.00	Reference		1.00	Reference	
Radical/total prostatectomy	0.18	0.17–0.19	<.001	0.13	0.11–0.14	<.001
Other cancer-directed surgery	0.79	0.76–0.82	<.001	0.78	0.75–0.81	<.001
Beam radiation						
No	1.00	Reference		1.00	Reference	
Yes	0.82	0.79–0.86	<.001	0.87	0.83–0.91	<.001

Stage IV with distant metastases at diagnosis (n = 14 417)

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Characteristics	All Causes of Death			Prostate Cancer-Specific Death		
	aHR*	95% CI	P	aHR*	95% CI	P
Time of diagnosis						
1988–1992	1.00	Reference		1.00	Reference	
1993–1997	0.98	0.94–1.02	.356	0.98	0.93–1.03	.355
1998–2003	1.00	0.95–1.05	.999	1.02	0.96–1.07	.537
Age						
35–50 y	0.92	0.80–1.05	.199	1.20	1.05–1.38	.010
51–60 y	0.78	0.73–0.83	<.001	0.97	0.90–1.04	.336
61–70 y	0.78	0.75–0.82	<.001	0.92	0.88–0.96	<.001
71+ y	1.00	Reference		1.00	Reference	
Ethnicity/race						
White	1.00	Reference		1.00	Reference	
Black	1.12	1.07–1.17	<.001	1.06	1.00–1.12	.034
Other/unknown	0.74	0.69–0.80	<.001	0.69	0.63–0.75	<.001
Tumor grade						
Well-/moderately differentiated	1.00	Reference		1.00	Reference	
Poorly/undifferentiated	1.48	1.42–1.55	<.001	1.70	1.61–1.78	<.001
Unknown	1.89	1.80–1.98	<.001	2.06	1.94–2.18	<.001
Cancer-directed surgery						
None	1.00	Reference		1.00	Reference	
Radical/total prostatectomy	0.28	0.22–0.36	<.001	0.20	0.14–0.27	<.001
Other cancer-directed surgery	1.00	0.96–1.04	.976	1.00	0.96–1.06	.851
Beam radiation						
No	1.00	Reference		1.00	Reference	
Yes	1.06	1.01–1.11	.011	1.15	1.10–1.21	<.001

CI indicates confidence interval.

*
Adjusted hazard ratio (aHR) based on Cox proportional hazards model, adjusted for time period of diagnosis, age, ethnicity/race, tumor grade, and cancer-directed surgery and radiation.