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Trends in the Incidence of Fatal Prostate Cancer in the United States by Race

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Abstract

Background: Prostate-specific antigen (PSA) testing has dramatically changed the composition of prostate cancer (PCa), making it difficult to interpret incidence trends. New methods are needed to examine temporal trends in the incidence of clinically significant PCa and whether trends vary by race.
Objective: To conduct an in-depth analysis of incidence trends in clinically significant PCa, defined as cases in which PCa was the underlying cause of death within 10 yr of diagnosis.
Design, setting, and participants: We extracted incident PCa cases during the period 1975–2002 and associated causes of death and survival through 2012 from nine cancer registries in the population-based Surveillance Epidemiology and End Results program database.
Outcome measurements and statistical analysis: We applied joinpoint regression analysis to identify when significant changes in trends occurred and age–period–cohort models to examine longitudinal and cross-sectional trends in the incidence of fatal PCa.
Results and limitations: Among 51 680 fatal PCa cases, incidence increased 1% per year prior to 1992, declined 15% per year from 1992 to 1995, and further declined by 5% per year through 2002. Age-specific incidence rates of fatal disease decreased >2% per year among men aged ≥60 yr, yet rates remained relatively stable among men aged ≤55 yr. Fatal disease rates were >2-fold higher in black men compared with white men, a racial disparity that increased to 4.2-fold among younger men.
Conclusions: The incidence of fatal PCa substantially declined after widespread PSA screening and treatment advances. Nevertheless, rates of fatal disease among younger men have remained relatively stable, suggesting the need for additional attention to early onset PCa, especially among black men. The persistent black-to-white racial disparity observed in fatal PCa underscores the need for greater understanding of the causes of this difference so that strategies can be implemented to eliminate racial disparities.
Patient summary: We assessed how the incidence of ultimately fatal prostate cancer (PCa) changed over time. We found that the incidence of fatal PCa declined by >50% since the introduction of prostate-specific antigen testing and advances in treatment options; however, incidence rates among younger men remained relatively stable, and younger black men exhibited a 4.2-fold higher risk for fatal disease compared with white men.

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1. Introduction

Prostate cancer (PCa) is the most frequently diagnosed cancer among men in the United States, with 180 890 new cases estimated for 2016 [1]. Despite notable improvements in PCa mortality rates in the United States over the past few decades [2], it is estimated that 26 120 men (8% of male cancer deaths) will die from this disease in 2016 [1]. Racial disparities in PCa are higher than for any other malignancy, with black men exhibiting a 2.5-fold greater risk of death from PCa compared with white men [1,3].

There has been a substantial increase in PCa incidence rates in the United States over the past few decades largely due to the increased detection of asymptomatic disease, first through transurethral prostatectomy (TURP) for benign prostatic hyperplasia [4], followed by widespread prostate-specific antigen (PSA) testing beginning in 1986 [5,6]. The subsequent decrease in PCa incidence rates, attributed to depletion of the latent PCa reservoir in the population, rendered the now-familiar "spike" in overall PCa incidence rates [6].

Accurate interpretation of clinically significant PCa incidence trends has been difficult because of the high prevalence of indolent disease and changes in screening practices. A majority of studies examining PCa trends have focused on the date of death (mortality rate) as opposed to the date of diagnosis [7,8], which is a more applicable time metric for assessing disease trends during a period of clinical change. In addition, no study in the past decade examined trends using age–period–cohort analysis [9], likely because of unstable parameters resulting from the PCa incidence rate spike.

To overcome these problems and to provide an in-depth analysis of clinically significant PCa incidence trends and racial disparities, we assessed trends in the incidence of fatal PCa, defined as death from this disease within 10 yr of diagnosis [10].

2. Materials and methods

We obtained census population estimates, cancer incidence, mortality, and survival data for calendar years 1975 to 2012 from the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) SEER-9 registries, which cover approximately 10% of the US population. We selected incident cases diagnosed with PCa (*International Classification of Diseases for Oncology*, third edition, code C619) as the first primary malignant cancer from 1975 (the first year all SEER-9 registries were operational) through 2002. Men were excluded if diagnosis was based on autopsy reports or death certificate only ($n = 4137$), if follow-up time was unknown ($n = 890$), or if age at diagnosis was missing ($n = 15$). Men were defined as having fatal PCa when PCa was the underlying cause of death within 10 yr of diagnosis (follow-up through 2012). The 10-yr window was selected a priori based on empirical evidence from SEER data (80% of all PCa-specific deaths were captured) and literature review [10,11].

We calculated age-standardized incidence rates and age-specific incidence rates per 100 000 person-years. We conducted joinpoint analysis to identify when statistically significant changes in trends occurred and estimated the annual percentage change in rates between joinpoints using weighted least squares [12]. Age–period–cohort models of fatal PCa were conducted to further examine temporal trends by year of diagnosis and to distinguish between influences that occurred in specific time periods for all age groups (period effects) and effects associated with specific birth cohorts (generational effects) [13,14]. For these models, data were classified by 1-yr periods into 40 age groups (45–84 yr), 28 calendar periods (1975–2002), and 66 birth cohorts (1891–1956). We fitted cross-sectional age-specific rates based on the central 1988 calendar year. We calculated black-to-white incidence rate ratios to examine racial disparities by period and age at diagnosis (5-yr weighted average age groups) [14]. Last, we used a quadratic spline to fit instantaneous hazard rates of death from PCa (percentage dying of PCa per year among all PCa cases), stratified by race and year of diagnosis (1975–1988 vs 1989–2002).

In sensitivity analyses, we evaluated shortened (5-yr) and extended (15-yr) follow-up for cause-specific mortality to assess whether competing risks and lead time bias affected trends. We also evaluated variable lead time, for which we extended follow-up to 15 yr in the PSA era. To evaluate the robustness of our models, we (1) included men with metastatic disease in our case definition; (2) limited the case pool to men for whom PCa was the sole cancer diagnosis; (3) expanded the case pool to include all men diagnosed with PCa, regardless of cancer sequence; (4) used predicted 10-yr probabilities of death due to PCa for men who died from other causes; and (5) concatenated the SEER-9, -13, and -18 databases.

Statistical analyses were performed in Matlab version R2014b (MathWorks Inc, Natick, MA, USA). All statistical tests were two-sided, and P values <0.05 were considered statistically significant.

3. Results

Of the 309 289 men diagnosed with PCa during 1975–2002, fatal PCa accounted for 17% ($n = 51\,680$) of the cases. A total of 222 321 men (72%) with PCa died from any cause during any period of follow-up, and 150 565 of those deaths (68%) occurred within 10 yr of PCa diagnosis. During the 10-yr period following diagnosis, PCa was the most common cause of death (34%), followed by ischemic heart disease (24%) and cerebrovascular diseases (5%).

3.1. Fatal prostate cancer trends

Trends in age-standardized incidence rates of fatal PCa are shown in Figure 1A. Joinpoint regression analysis of trends by year of diagnosis identified two joinpoints, in 1992 and 1995 (Table 1), which indicated that rates of fatal PCa increased 1.0% per year from 1975 to 1992, declined 15.0% per year during the subsequent 3-yr period (1992–1995), and steadily declined by 5.0% per year through 2002. Age-specific rates of fatal PCa by year of diagnosis exhibited differences between older and younger men, such that rates among younger men appeared relatively stable, whereas rates in older men (aged ≥55 yr) revealed a declining trend beginning in the early 1990s (Fig. 1B).

Age–period–cohort models for fatal PCa were successfully fit. Age-specific annual percentage changes were heterogeneous (two-sided Wald test; $\chi^2 = 166.3$, $df = 40$, $p < 0.0001$) when compared with the overall annual percentage change of −1.77% per year. Rates among younger men (aged ≤52 yr) increased by up to 0.6% per year, whereas rates decreased for older men (aged ≥61 yr) by >2% per year (Supplementary Fig. 1). Period rate ratios demonstrated a significant decline in risk of fatal disease

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