Racial differences in PSA screening interval and stage at diagnosis

William R. Carpenter,
Department of Health Policy and Management, Gillings School of Global Public Health, University of North Carolina (UNC), 1102F McGavran Greenberg Hall; CB 7411, Chapel Hill, NC 27599, USA

UNC Lineberger Comprehensive Cancer Center, UNC Chapel Hill, Chapel Hill, NC, USA

UNC Cecil G. Sheps Center for Health Services Research, Raleigh, NC, USA

North Carolina Comprehensive Cancer Program, Raleigh, NC, USA

Institute for Health, Social and Community Research, Shaw University, Raleigh, NC, USA

Daniel L. Howard,
Institute for Health, Social and Community Research, Shaw University, Raleigh, NC, USA

Yhenneko J. Taylor,
Institute for Health, Social and Community Research, Shaw University, Raleigh, NC, USA

Louie E. Ross,
Institute for Health, Social and Community Research, Shaw University, Raleigh, NC, USA

Sara E. Wobker, and
UNC Lineberger Comprehensive Cancer Center, UNC Chapel Hill, Chapel Hill, NC, USA

Paul A. Godley
Department of Health Policy and Management, Gillings School of Global Public Health, University of North Carolina (UNC), 1102F McGavran Greenberg Hall; CB 7411, Chapel Hill, NC 27599, USA

UNC Lineberger Comprehensive Cancer Center, UNC Chapel Hill, Chapel Hill, NC, USA

UNC Cecil G. Sheps Center for Health Services Research, Raleigh, NC, USA

Division of Hematology/Oncology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Abstract

Objectives—This study examined PSA screening interval of black and white men aged 65 or older and its association with prostate cancer stage at diagnosis.

Methods—SEER-Medicare data were examined for 18,067 black and white men diagnosed with prostate cancer between 1994 and 2002. Logistic regression was used to assess the association between race, PSA screening interval, and stage at diagnosis. Analysis also controlled for age, marital status, comorbidity, diagnosis year, geographic region, income, and receipt of surgery.

Results—Compared to whites, blacks diagnosed with prostate cancer were more likely to have had a longer PSA screening interval prior to diagnosis, including a greater likelihood of no pre-diagnosis use of PSA screening. Controlling for PSA screening interval was associated with a reduction in blacks' relative odds of being diagnosed with advanced (stage III or IV) prostate cancer, to a point

that the stage at diagnosis was not statistically different from that of whites (OR=1.12, 95% CI=0.98–1.29). Longer intra-PSA intervals were systematically associated with greater odds of diagnosis with advanced disease.

Conclusions—More frequent or systematic PSA screening may be a pathway to reducing racial differences in prostate cancer stage at diagnosis, and, by extension, mortality.

Introduction

Prostate cancer is the most commonly diagnosed non-cutaneous malignancy in American men, with approximately 192,000 new cases and 27,000 prostate cancer deaths in 2009 [1]. Black men suffer a disproportionate burden from the disease, with 1.6 times greater incidence and 2.4 times greater mortality than that of white [2]. Investigators have examined clinical and sociodemographic factors, access to and utilization of early detection and treatment, and tumor characteristics as possible explanations for the tremendous disparity in prostate cancer mortality; [3–8] however, the underlying causes of the racial disparity remain poorly understood. Biological factors, including genetics and dietary differences, may play a role in the racial disparity [9–12]. Until there is more evidence of the relative impact of these factors, examining the use of early detection and its effectiveness remains critical.

Stage at diagnosis is strongly associated with survival [13,14], and early detection has proved successful in reducing mortality from other cancers, such as breast, colorectal, and cervical [15–17]. The prostate-specific antigen (PSA) test is commonly used for screening for prostate cancer and has contributed to a dramatic increase in disease detection [18]. Observational studies have shown a reduction in prostate cancer-specific mortality in men who undergo PSA testing [19–21], but recent results from two large randomized controlled trials have not consistently supported the role of PSA in reducing mortality. The Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial included over 75,000 American men with 7–10 years of follow-up and found no significant difference in mortality rates [22]. The European Randomized Study of Screening for Prostate Cancer included over 165,000 men with an average of 9 years of follow-up, and resulted in a 20% decrease in mortality, but at the cost of increased risk of overdiagnosis [23].

However, neither of these studies included a sufficient number of black men to analyze differences by race, so any benefit of PSA in this population remains unclear. Studies have found an association between serial PSA screening and a decrease in clinically advanced and high grade disease [24], stage migration from distant to earlier stages [25,26], and an evolution toward earlier pathologic stage, grade, and PSA outcome [27]. Meanwhile, blacks continue to be more commonly diagnosed with higher stage and grade tumors than their white counterparts [28].

Better understanding of racial differences in the use of early detection and the associated stage at diagnosis may contribute to understanding the racial disparity in prostate cancer mortality. As a result of differences in clinical and sociodemographic factors and tumor biology between races, optimal PSA screening interval may differ by race, and this difference may be associated with the racial disparity in stage at diagnosis. In completed studies of PSA screening interval, it has been shown that a shorter interval is associated with earlier stage and less severe grade at diagnosis [29,30]. This study examines PSA screening interval as it is associated with racial differences in prostate cancer stage at diagnosis among a group of black and white men aged 65 or older.

Methods

Data are from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database, described in detail elsewhere [31]. Briefly, SEER-Medicare is a collaborative effort between the National Cancer Institute's SEER program and the Medicare program, offering a comprehensive dataset of cancer diagnosis and treatments as well as other diseases and conditions that may influence treatment and survival. The eight SEER registries used in this study represent 11% of the US population.

Each registry collects data on newly diagnosed cases of cancer including histology, grade, stage, and treatment, as well as patient demographic characteristics, follow-up of vital status, and cause of death (if applicable). Medicare provides health insurance coverage to approximately 97% of Americans 65 years of age or older. Medicare data reflect diagnoses and health services provided to beneficiaries by physicians, hospitals, home health care agencies, nursing facilities, and hospice programs.

Study population

Data from the SEER-Medicare linked database were examined for black and white men diagnosed with prostate cancer between 1994 and 2002 from the following eight SEER registries: Atlanta, Connecticut, Detroit, Rural Georgia, Los Angeles, San Francisco-Oakland, San Jose, and Seattle-Puget Sound. Men were included if they were aged 65 or older at diagnosis, had known prostate cancer stage, had no prior or concurrent cancers, no gaps in Medicare coverage from enrollment to diagnosis, continuous coverage for 3 years prior to diagnosis, and no HMO coverage from enrollment to diagnosis.

Measurement of variables

The primary study outcome, tumor stage at diagnosis, was obtained from SEER data. Tumor stage was based on the American Joint Committee on Cancer (AJCC) staging criteria and classified as early stage (stage 1 or 2) or advanced stage (stage 3 or 4). Histological grade was classified in the SEER data, based on Gleason score, as well-differentiated (2–4), moderately differentiated (5–7), poorly differentiated (8–10), or undifferentiated/anaplastic [32]. For the purposes of this analysis, poorly ($n = 4,321$) and undifferentiated ($n = 72$) tumors were combined into a single category.

Time since last PSA test was ascertained from Medicare claims data using Healthcare Common Procedure Coding System (HCPCS) codes 84153, 84154, 86316, and G0103 to identify PSA tests. Only PSA tests occurring greater than 2 months, prior diagnosis month was included in order to avoid inclusion of repeat PSA tests used as a part of patient diagnostic workup [33]. Patient race (black or white), age (65–69, 70–74, 75–79, 80+), marital status, and year of diagnosis were also obtained from SEER data. A comorbidity index score was calculated for each patient using Medicare claims up to 12 months prior to diagnosis date in an algorithm developed specifically for use with SEER-Medicare data [34]. For cancers diagnosed prior to 1998, surgical procedures were evaluated using SEER site-specific surgery codes 10–29 for transurethral resection of the prostate (TURP), 30–99 for prostatectomy and 01–06 for biopsy. Reflecting a coding system change, for diagnosis years 1998 and onward we used SEER surgery of the primary site codes 10–17 for TURP, and 30–98 for prostatectomy. Zip code-level aggregate indicators of education and income from the 2000 census were examined as quartiles based on the analytic sample.

Analysis

Descriptive analyses were performed to assess patient characteristics by race and time interval since last PSA test. Chi-square tests were used for bivariate comparisons of patient

characteristics by race. Multivariate logistic regression was used to examine associations between race, screening interval, and cancer stage at diagnosis. Models were examined sequentially to assess the baseline racial differences in stage at diagnosis, the differences when controlling for potential confounders ("fully specified"), and effect of adding screening interval to the fully specified model. In the baseline model (Table 2, Model 1) SEER site was retained to control for obvious regional differences, including that a substantial portion of the overall black sample resided in Detroit, and that population's systematically different use of PSA compared to black's in other SEER regions. The fully specified model included age at diagnosis, marital status, diagnosis year, comorbidity score, median household income, and receipt of surgery/related procedure as covariates. Receipt of surgery was included in regression models to account for the possibility of tumor upstaging in men who underwent prostatectomy, and comorbidity was included to control for differential exposure to health care services, including PSA tests resulting from comorbid or ongoing health conditions.

Multiple sensitivity analyses and model specification tests were conducted. Among them, interactions between race and screening interval were assessed (and found to be non-significant). Additional sensitivity analyses were conducted examining asymptomatic and symptomatic PSAs independently and then all PSAs regardless of corresponding symptoms or diagnosis. For these analyses, PSA tests were categorized as symptomatic if a diagnosis code for any lower urinary tract symptoms (LUTS) was included on insurance claims within 30 days prior to 7 days post-PSA claim date, and as asymptomatic if no LUTS were included on claims within the specified window. All statistical tests were two-sided with a significance level of 0.05. All analyses were conducted using SAS® Version 9.1 (SAS Institute, Cary, NC).

Results

The analytic sample included 18,067 men (15.8% black and 84.2% white), as presented in Table 1. The mean age was 74.7 (standard deviation (SD) = 5.9) for blacks and 75.4 (SD = 5.7) for whites. Many men had undergone PSA testing within a year prior to diagnosis, though whites were more likely to have done so (blacks: 40.4%; whites 46.1%). Blacks were more likely than whites to have had no PSA tests prior to diagnosis (black: 32.8%, white: 22.1%; $p < 0.001$). Screening intervals also varied by cancer stage; men diagnosed with advanced-stage tumors were more likely to have no PSA tests prior to diagnosis (advanced: 36.9%; early: 19.6%) and less likely to have been tested within a year of diagnosis (advanced: 34.4%; early: 48.6%) than those with early stage tumors (data not shown). Compared to white men, black men in our sample were less likely to be married and were more likely to live in areas with lower average education levels and lower median household income (Table 1). Significantly more black (52.8%) than white (29.6%) men were from the Detroit SEER region, which included the largest fraction of black men in the study sample. Black men had greater comorbidity, as reflected by a higher percentage with a comorbidity score of 1 or higher (38.6 vs. 29.6%, $p < 0.001$). Overall unadjusted rates of early versus advanced stage at diagnosis were comparable between black and white men. Over 60% of men in the sample had undergone a surgery-related procedure with 16.9 and 10.8% of white and black men, respectively, having undergone a prostatectomy.

Several differences were noted between demographic characteristics of blacks and whites within the same PSA testing intervals (data not shown). Blacks in the 3–12-month interval and those with no PSA tests prior to diagnosis were younger than their white counterparts. The percent of whites and blacks in the no PSA testing group declined over time; however, significantly more whites than blacks with no prior PSA test had been diagnosed prior to 1996 (44.8 vs. 36.7%). Additionally, blacks in all testing intervals were less likely to be married and resided in zip code areas with higher percentages of less than high school graduates and lower median household incomes than whites. Examination of clinical characteristics by race and

PSA screening interval showed that blacks were consistently more likely than whites to have one or more comorbidities. Among those who had a PSA test prior to prostate cancer diagnosis, blacks were more likely than whites to have no urinary symptoms at the time of their last PSA test.

Multivariate logistic regression analysis of cancer stage at diagnosis revealed that blacks had higher odds of advanced-stage versus early stage cancer at diagnosis than did whites (odds ratio (OR) = 1.24, 95% CI: 1.13–1.37) than whites (Table 2, Model 1). A more fully specified model, including multiple confounders, resulted in a non-significant decline in the racial difference (OR=1.21, 95% CI: 1.06–1.39). Further controlling for PSA screening interval in this model resulted in a 7% decrease in odds of being diagnosed with advanced-stage cancer compared to the base model (OR=1.12, 95% CI=0.98–1.29), and the difference between blacks and whites was no longer statistically significant. The more fully specified model adjusting for race, screening interval, SEER site, age, marital status, comorbidity score, diagnosis year, income, and receipt/type of surgery showed an association between screening interval and odds of advanced-stage cancer that was both persistent and in the hypothesized direction. That is, greater time since the last PSA was systematically associated with a greater probability of being diagnosed with advanced disease, while the independent association with race remained non-significant. Those with no prior history of PSA in their Medicare claims were nearly three times more likely to be diagnosed with advanced disease than those who had their most recent PSA one year or less prior to diagnosis. More recent diagnosis years were associated with lower odds of advanced-stage cancers, as were living in a higher income area and being married.

Discussion

To elucidate factors that may contribute to the tremendous racial disparity in prostate cancer mortality, this study examined the association between PSA screening interval and stage at diagnosis in a large sample of older black and white men with prostate cancer. In this population, overall and race-specific stage at diagnosis are reflective of the overall national trends in stage at diagnosis. Unadjusted data in this study present equivalent stage groupings at diagnosis (Stage I/II, Stage III/IV), though national data present black men as having slightly greater rates of diagnosis with metastatic disease [2]. When controlling for multiple confounders, black men in this study population were more likely than white men to be diagnosed with advanced disease. The length of the pre-diagnosis PSA screening interval was strongly associated with stage at diagnosis, and its inclusion in the analysis was associated with substantial attenuation in racial differences in stage at diagnosis. Specifically, when controlling for screening interval, there was no statistical difference between black and white men's stage at diagnosis. In contrast, the addition of multiple, often-studied covariates (age, marital status, year of diagnosis, income, comorbidity, surgery/surgery type) was associated with only limited change in the relationship between race, screening interval, and stage at diagnosis. These associations suggest that screening interval may be a relevant factor in explaining racial differences in prostate cancer outcomes, perhaps as a function of the greater number of treatment options and typically better outcomes associated with early stage diagnosis.

Variation among SEER regions was notable in terms of both PSA screening use and stage at diagnosis, likely based on regional differences in care patterns. For example, the Detroit SEER region includes approximately 50% of the black men in our sample, and in this sample the distribution of screening interval among blacks was similar to the screening interval of whites residing not only in Detroit but also to whites in the rest of the study sample. These systematic geographic differences mandated controlling for region in all analyses and point to an area of opportunity for further, closer study, as the different health care patterns and outcomes could result from many factors. Among them, it may be that blacks in Detroit span a wider spectrum of socioeconomic status, which may contrast with other SEER regions such as Connecticut or

Seattle, in which the smaller black population may be much less diverse such that a higher screening population is not well represented. There may also be different social norms among blacks in this region that are associated with greater use of health care in general, and preventive health care specifically. Alternatively, it may be that there are unique organizational characteristics or a prevention orientation of a dominant health system in this geographically small region. Understanding these factors may elucidate a model for other health systems in other regions to follow.

The effectiveness of PSA screening in terms of reducing prostate cancer mortality remains controversial;[35,36] however, these findings support the hypothesis that screening interval plays a role in racial disparities in the stage of disease at diagnosis, so addressing differences in screening practices may reduce disparities in mortality. Previous work suggests that racial differences in the use of prostate cancer early detection are a function of differences in individuals' usual source of care and associated variation in patient–provider interactions, and health care systems and processes [37,38]. These studies document substantial differences in pre-diagnosis prostate cancer screening use among men diagnosed with prostate cancer depending on the continuity of care and the usual source of care (e.g., private practice, hospital clinic, community health clinic, emergency room, etc.), and posit that physician biases and practical constraints that differ by source of regular care may inhibit physicians' and patients' ability to inquire beyond the primary issue at hand to preventive health issues and secondary or more complex issues. Moreover, these differences are likely to vary systematically according to the systems in place at the care sites that serve as individuals' usual sources of care. This study reinforces these earlier findings by demonstrating lower and less frequent use of PSA screening by blacks compared to whites and racial differences in stage at diagnosis. Substantial regional variation in pre-diagnosis prostate cancer screening suggests merit in a more extensive examination of racial differences in prostate cancer incidence and mortality in terms of the usual source of care, the continuity and quality of physician-patient interaction, differential use of prostate cancer early detection, and stage and grade at diagnosis.

These study results suggest a pathway to reducing the racial differences in the initial prostate cancer stage through a decrease in the PSA screening intervals—that is, more and more frequent use of PSA screening—among black. However, while this study found an association between screening interval and racial disparities in the stage at diagnosis, it does not fully address racial differences in cancer aggressiveness, which arguably may be a more important predictor of prostate cancer outcomes, a point amplified by a recent study by Albain and colleagues demonstrating the persistence of racial mortality differences among white and black men with similarly advanced-stage prostate cancer [39]. This study lends insight into racial differences in screening and stage at diagnosis, but does not address the overall question of whether PSA screening is effective in reducing prostate cancer mortality among blacks at any screening interval. With this regard, PSA effectiveness may also differ by race, an association that was not evaluated by the PLCO and European studies [22,23].

The issue of racial differences in PSA testing compounds the already complex issue of PSA screening in general, as health care scientists and clinicians continue to examine several variations of PSA testing, including the distributions of total PSA, free PSA, percent free PSA, and others. PSA level varies with age and race-ethnicity among American men and may lead to different thresholds of PSA tests and perhaps different screening intervals [40]. Patients diagnosed by annual prostate cancer screening appeared more likely to experience an indolent PSA recurrence and less likely to die of prostate cancer after PSA recurrence compared with patients referred from the community [41]. A single PSA test taken at or before age 50 is a very strong predictor of advanced prostate cancer diagnosed up to 25 years later. This suggests the possibility of using an early PSA test to risk-stratify patients so that men at highest risk are

the focus of the most intensive screening efforts, an intervention that would need to be tested in a controlled trial [42].

The use of administrative claims-based data allowed the examination of a substantially larger population than would be feasible through an interview- or medical records-based study; however, the health services documented in the data only reflect those that have an associated procedure code and are reimbursed by Medicare. As such, these data would not capture a PSA that was provided and not billed for, such as through a free community screening event. Perhaps more importantly, because digital rectal examinations (DRE) are commonly considered a part of the regular office visit and not consistently billed for independently, these data do not reliably reflect its use and so it was excluded from the analysis; however, DRE has not been shown to prevent cancer-related deaths. This being said, all individuals in this study were enrolled continuously in Medicare, reflecting at least a stable baseline set of health care resources. Finally, Medicare did not reimburse for screening PSA prior to the year 2000, and so the presence of PSA in Medicare claims prior to this point and the validity of associated diagnoses or symptoms (i.e., such as would differentiate between asymptomatic screening, or symptomatic testing) are unknown and likely to be variable.

Conclusion

For the general public and medical and public health practitioners, this study's results are promising and complement prior research demonstrating variation in pre-diagnosis screening use among differing levels of care continuity and different sources of regular care. Together, they suggest merit in additional research integrating the study of prostate cancer screening intervals, care continuity and usual source of care, and stage and grade at diagnosis as they may differ by race. Biological differences may be contributing to prostate cancer outcomes, but at least a portion of the racial disparity in prostate cancer mortality may be resolved by addressing the care systems and care continuity among care providers where black men are more likely than white men to seek regular care. The association between increasing screening interval and progressively increased risk of diagnosis with advanced disease informs the research community regarding appropriate prostate cancer screening interval for all men, including the prospect of screening recommendations that may differ according to different personal risk levels.

Compared to other cancers, many aspects of prostate cancer remain an enigma, not the least of which concerns the appropriate use of screening and early detection, particularly given the debate surrounding its efficacy. What remains clear is that there is much to learn regarding both biological and sociological characteristics influencing the etiology of the disease, efficacy and appropriate use of early detection, and treatment decisions that appropriately balance maximizing survival while minimizing the risk of unnecessary or excessive treatment risks and side effects. The extraordinary racial disparities in incidence and especially mortality place a premium on each new discovery and piece of new information.

Acknowledgments

References

1. American Cancer Society. Cancer facts & figures 2009. American Cancer Society; Atlanta: 2009.

2. American Cancer Society. Cancer facts and figures for African Americans, 2009-10. American Cancer Society; Atlanta: 2009.

3. Institute of Medicine. Unequal treatment: confronting racial and ethnic disparities in healthcare. National Academies Press; Washington DC: 2003.

4. Institute of Medicine. The unequal burden of cancer: as assessment of NIH research and programs for ethnic minorities and the medically underserved. National Academies Press; Washington DC: 1999.

5. Bach PB, Cramer LD, Warren JL, Begg CB. Racial differences in the treatment of early-stage lung cancer. N Engl J Med 1999;341(16):1198–1205. [PubMed: 10519898]

6. Field TS, Buist DS, Doubeni C, et al. Disparities and survival among breast cancer patients. J Natl Cancer Inst Monogr 2005;(35):88–95. [PubMed: 16287892]

7. Harlan L, Brawley O, Pommerenke F, Wali P, Kramer B. Geographic, age, and racial variation in the treatment of local/regional carcinoma of the prostate. J Clin Oncol 1995;13(1):93–100. [PubMed: 7799048]

8. Gilligan T, Wang PS, Levin R, Kantoff PW, Avorn J. Racial differences in screening for prostate cancer in the elderly. Arch Intern Med 2004;164(17):1858–1864. [PubMed: 15451760]

9. Giovannucci E, Stampfer MJ, Krithivas K, et al. The CAG repeat within the androgen receptor gene and its relationship to prostate cancer. Proc Natl Acad Sci USA 1997;94(7):3320–3323. [PubMed: 9096391]

10. Hayes RB, Ziegler RG, Gridley G, et al. Dietary factors and risks for prostate cancer among blacks and whites in the United States. Cancer Epidemiol Biomarkers Prev 1999;8(1):25–34. [PubMed: 9950236]

11. Lichtenstein P, Holm NV, Verkasalo PK, et al. Environmental and heritable factors in the causation of cancer–analyses of cohorts of twins from Sweden, Denmark, and Finland. N Engl J Med 2000;343 (2):78–85. [PubMed: 10891514]

12. Moul JW, Sesterhenn IA, Connelly RR, et al. Prostate-specific antigen values at the time of prostate cancer diagnosis in African-American men. JAMA 1995;274(16):1277–1281. [PubMed: 7563532]

13. Johansson JE, Holmberg L, Johansson S, Bergstrom R, Adami HO. Fifteen-year survival in prostate cancer. A prospective, population-based study in Sweden. JAMA 1997;277(6):467–471. [PubMed: 9020270]

14. Jonsson E, Sigbjarnarson HP, Tomasson J, et al. Adeno-carcinoma of the prostate in Iceland: a population-based study of stage, Gleason grade, treatment and long-term survival in males diagnosed between 1983 and 1987. Scand J Urol Nephrol 2006;40(4):265–271. [PubMed: 16916765]

15. Tabar L, Fagerberg CJ, Gad A, et al. Reduction in mortality from breast cancer after mass screening with mammography. Randomised trial from the breast cancer screening working group of the Swedish national board of health and welfare. Lancet 1985;1(8433):829–832. [PubMed: 2858707]

16. Mandel JS, Bond JH, Church TR, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. N Engl J Med 1993;328(19):1365–1371. [PubMed: 8474513]

17. Laara E, Day NE, Hakama M. Trends in mortality from cervical cancer in the Nordic countries: association with organised screening programmes. Lancet 1987;1(8544):1247–1249. [PubMed: 2884378]

18. Amling CL. Prostate-specific antigen and detection of prostate cancer: what have we learned and what should we recommend for screening? Curr Treat Options Oncol 2006;7(5):337–345. [PubMed: 16904050]

19. Agalliu I, Weiss NS, Lin DW, Stanford JL. Prostate cancer mortality in relation to screening by prostate-specific antigen testing and digital rectal examination: a population-based study in middle-aged men. Cancer Causes Control 2007;18(9):931–937. [PubMed: 17641982]

20. Weinmann S, Richert-Boe K, Glass AG, Weiss NS. Prostate cancer screening and mortality: a case-control study (United States). Cancer Causes Control 2004;15(2):133–138. [PubMed: 15017125]

21. Oberaigner W, Horninger W, Klocker H, Schonitzer D, Stuhlinger W, Bartsch G. Reduction of prostate cancer mortality in Tyrol, Austria, after introduction of prostate-specific antigen testing. Am J Epidemiol 2006;164(4):376–384. [PubMed: 16829552]

22. Andriole GL, Crawford ED, Grubb RL III, et al. Mortality results from a randomized prostate-cancer screening trial. N Engl J Med 2009;360(13):1310–1319. [PubMed: 19297565]

23. Schroder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized European study. N Engl J Med 2009;360(13):1320–1328. [PubMed: 19297566]

24. Smith DS, Catalona WJ, Herschman JD. Longitudinal screening for prostate cancer with prostate-specific antigen. JAMA 1996;276(16):1309–1315. [PubMed: 8861989]

25. Gilliland FD, Hunt WC, Key CR. Improving survival for patients with prostate cancer diagnosed in the prostate-specific antigen era. Urology 1996;48(1):67–71. [PubMed: 8693654]

26. Hugosson J, Aus G, Lilja H, Lodding P, Pihl CG. Results of a randomized, population-based study of biennial screening using serum prostate-specific antigen measurement to detect prostate carcinoma. Cancer 2004;100(7):1397–1405. [PubMed: 15042673]

27. Ung JO, Richie JP, Chen MH, Renshaw AA, D'Amico AV. Evolution of the presentation and pathologic and biochemical outcomes after radical prostatectomy for patients with clinically localized prostate cancer diagnosed during the PSA era. Urology 2002;60(3):458–463. [PubMed: 12350484]

28. Virnig BA, Baxter NN, Habermann EB, Feldman RD, Bradley CJ. A matter of race: early-versus late-stage cancer diagnosis. Health Aff (Millwood) 2009;28(1):160–168. [PubMed: 19124866]

29. Hugosson J, Aus G, Bergdahl S, et al. Population-based screening for prostate cancer by measuring free and total serum prostate-specific antigen in Sweden. BJU Int 2003;92(Suppl 2):39–43. [PubMed: 14983953]

30. Kundu SD, Grubb RL, Roehl KA, Antenor JA, Han M, Catalona WJ. Delays in cancer detection using 2 and 4-year screening intervals for prostate cancer screening with initial prostate specific antigen less than 2 ng/ml. J Urol 2005;173(4):1116–1120. [PubMed: 15758718]

31. Warren JL, Klabunde CN, Schrag D, et al. Overview of the SEER-Medicare data: content, research applications, and generalizability to the United States elderly population. Med Care 2002;40:3–18.

32. Fritz, A.; Ries, L., editors. The SEER program code manual. 3rd edn.. National Cancer Institute; Bethesda, MD: 1998.

33. Yao SL, Lu-Yao G. Interval after prostate specific antigen testing and subsequent risk of incurable prostate cancer. J Urol 2001;166:861–865. [PubMed: 11490234]

34. Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. J.Clin Epidemiol 2000;53:1258–1267. [PubMed: 11146273]

35. Barry MJ. Screening for prostate cancer—the controversy that refuses to die. NEJM 2009;360(13): 1351–1354. [PubMed: 19297564]

36. Zoorob R, Anderson R, Cefalu C, Sidani M. Cancer screening guidelines. Am Fam Physician 2001;63 (6):1101–1112. [PubMed: 11277547]

37. Carpenter WR, Godley PA, Finnegan T, Talcott JA, Clark JA, Mishel M, Schroeder JC, Bensen JT, Su JL, Fontham ETH, Mohler JL. Racial differences in the roles of trust, regular source of patient care, and screening and treatment utilization among individuals with prostate cancer. Cancer 2009;155(21):5048–5059. [PubMed: 19637357]

38. Talcott JA, Spain P, Clark JA, Carpenter WR, Do YK, Hamilton RJ, Galanko JA, Jackman A, Godley PA. Hidden barriers between knowledge and behavior: the North Carolina prostate cancer screening and treatment experience. Cancer 2007;109(8):1599–1606. [PubMed: 17354220]

39. Albain KS, Unger JM, Crowley JJ, Coltman CA Jr, Hershman DL. Racial disparities in cancer survival among randomized clinical trials patients of the Southwest oncology group. JNCI 2009;101(14):984–992. [PubMed: 19584328]

40. Lacher DA, Thompson TD, Hughes JP, Saraiya M. Total, free, and percent free prostate-specific antigen levels among US men, 2001–04. Adv Data 2006;379:1–12. [PubMed: 17348177]

41. Efstathiou JA, Chen MH, Catalona WJ, et al. Prostate-specific antigen-based serial screening may decrease prostate cancer-specific mortality. Urology 2006;68(2):342–347. [PubMed: 16904449]

42. Ulmert D, Cronin AM, Bjork T, et al. Prostate-specific antigen at or before age 50 as a predictor of advanced prostate cancer diagnosed up to 25 years later: a case-control study. BMC Med 2008;6:6. [PubMed: 18279502]

Table 1

Demographic and clinical characteristics by race for men diagnosed with stage 1–4 prostate cancer, SEER-Medicare 1994–2002

Characteristics	n(% of column)			p[a]
	Total n = 18,067	White n = 15,219	Black n = 2,848	
Months since last PSA				<0.001
3–12	8,164(45.2)	7,013(46.1)	1,151(40.4)	
13–24	3,190(17.7)	2,796(18.4)	394(13.8)	
25–36	1,104(6.1)	953(6.3)	151(5.3)	
37–128	1,317(7.3)	1,099(7.2)	218(7.7)	
No PSA	4,292(23.8)	3,358(22.1)	934(32.8)	
Cancer stage				0.999
Early stage (stage 1–2)	13,734(76.0)	11,569(76.0)	2,165(76.0)	
Advanced stage (stage 3–4)	4,333(24.0)	3,650(24.0)	683(24.0)	
Histological grade				<0.001
Well differentiated	218(1.2)	196(1.3)	22(0.8)	
Moderately differentiated	12,896(71.4)	10,948(71.9)	1,948(68.4)	
Poorly differentiated	4,393(24.3)	3,628(23.8)	765(26.9)	
Unknown	560(3.1)	447(2.9)	113(4.0)	
Age at diagnosis				<0.001
65–69	2,997(16.6)	2,401(15.8)	596(20.9)	
70–74	6,211(34.4)	5,223(34.3)	988(34.7)	
75–79	4,966(27.5)	4,256(28.0)	710(24.9)	
80+	3,893(21.5)	3,339(21.9)	554(19.5)	
Married				<0.001
Yes	12,431(68.8)	10,903(71.6)	1,528(53.7)	
No	4,617(25.6)	3,499(23.0)	1,118(39.3)	
Unknown	1,019(5.6)	817(5.4)	202(7.1)	
Diagnosis year				0.043
1994	2,687(14.9)	2,306(15.2)	381(13.4)	
1995	2,276(12.6)	1,933(12.7)	343(12.0)	
1996	2,177(12.0)	1,800(11.8)	377(13.2)	
1997	2,124(11.8)	1,761(11.6)	363(12.7)	
1998	1,968(10.9)	1,667(11.0)	301(10.6)	
1999	1,873(10.4)	1,570(10.3)	303(10.6)	
2000	1,784(9.9)	1,496(9.8)	288(10.1)	
2001	1,664(9.2)	1,422(9.3)	242(8.5)	
2002	1,514(8.4)	1,264(8.3)	250(8.8)	
SEER site				<0.001
Atlanta	1,507(8.3)	1,084(7.1)	423(14.9)	
Connecticut	3,139(17.4)	2,959(19.4)	180(6.3)	
Detroit	5,475(30.3)	3,971(26.1)	1,504(52.8)	
Los Angeles	2,445(13.5)	2,089(13.7)	356(12.5)	

Characteristics	n(% of column)			p^a
	Total n = 18,067	White n = 15,219	Black n = 2,848	
Rural Georgia	95(0.5)	50(0.3)	45(1.6)	
San Francisco	1,564(8.7)	1,329(8.7)	235(8.3)	
San Jose	929(5.1)	899(5.9)	30(1.1)	
Seattle	2,913(16.1)	2,838(18.6)	75(2.6)	
Zip code % non-high school graduates				<0.001
0–8.4%	4,311(23.9)	4,228(27.8)	83(2.9)	
8.5–13.6%	4,422(24.5)	4,249(27.9)	173(6.1)	
13.7–21.5%	4,326(23.9)	3,788(24.9)	538(18.9)	
21.6–100%	4,326(23.9)	2,341(15.4)	1,985(69.7)	
Unknown	682(3.8)	613(4.0)	69(2.4)	
Zip code median household income				<0.001
≤$41,302	4,350(24.1)	2,208(14.5)	2,142(75.2)	
$41,303–$51,222	4,351(24.1)	3,994(26.2)	357(12.5)	
$51,223–$64,833	4,340(24.0)	4,125(27.1)	215(7.5)	
$64,834–$200,008	4,344(24.0)	4,279(28.1)	65(2.3)	
Unknown	682(3.8)	613(4.0)	69(2.4)	
Comorbidity score				<0.001
0	11,787(65.2)	10,293(67.6)	1,494(52.5)	
1	3,692(20.4)	3,031(19.9)	661(23.2)	
2+	1,907(10.6)	1,468(9.6)	439(15.4)	
Unknown	681(3.8)	427(2.8)	254(8.9)	
Symptoms at last PSA				<0.001
Hematuria/vascular disorders	437(2.4)	355(2.3)	82(2.9)	
Other urinary symptoms (not hematuria)	7,763(43.0)	6,841(45.0)	922(32.4)	
No urinary symptoms	5,575(30.9)	4,665(30.7)	910(32.0)	
No PSA	4,292(23.8)	3,358(22.1)	934(32.8)	
Surgery type				<0.001
Exploratory Biopsy	5,419(30.0)	4,573(30.0)	846(29.7)	
TURP	2,820(15.6)	2,319(15.2)	501(17.6)	
Prostatectomy	2,877(15.9)	2,570(16.9)	307(10.8)	

Per SEER-Medicare policy, to protect confidentiality, the count of 'unknowns' for some variables is not presented

[a] p-value comparing characteristics of black and white men obtained from Chi-square test TURP=transurethral resection of the prostate

Table 2

Multivariate logistic regression of odds of advanced vs. early stage prostate cancer at diagnosis, SEER-Medicare 1994–2002

Effect	Model 1		Model 2		Model 3	
	OR(95% CI)	p	OR(95% CI)	p	OR(95% CI)	p
Race		<0.001		0.006		0.108
White	ref		ref		ref	
Black	1.24(1.13–1.37)		1.21(1.06–1.39)		1.12(0.98–1.29)	
Months since last PSA						<0.001
3–12					ref	
13–24					1.18(1.05–1.33)	
25–36					1.37(1.15–1.63)	
37–128					2.21(1.89–2.59)	
No PSA					2.77(2.49–3.07)	
SEER site		<0.001		<0.001		<0.001
Atlanta	ref		ref		ref	
Connecticut	1.16(1.00–1.35)		1.40(1.17–1.67)		1.24(1.03–1.49)	
Detroit	0.76(0.66–0.87)		0.86(0.73–1.02)		0.92(0.77–1.09)	
Los Angeles	1.59(1.37–1.86)		1.35(1.12–1.62)		1.44(1.20–1.73)	
Rural Georgia	1.41(0.89–2.25)		1.42(0.84–2.41)		1.43(0.84–2.42)	
San Francisco	1.48(1.25–1.74)		1.37(1.12–1.67)		1.37(1.12–1.68)	
San Jose	1.46(1.21–1.77)		1.54(1.23–1.94)		1.53(1.21–1.93)	
Seattle	1.84(1.59–2.14)		1.62(1.35–1.94)		1.61(1.34–1.94)	
Diagnosis year				<0.001		<0.001
1994			ref		ref	
1995			0.85(0.74–0.97)		0.90(0.78–1.04)	
1996			0.58(0.50–0.67)		0.65(0.56–0.75)	
1997			0.57(0.49–0.66)		0.65(0.55–0.76)	
1998			0.51(0.43–0.60)		0.59(0.50–0.71)	
1999			0.45(0.37–0.54)		0.52(0.44–0.63)	
2000			0.38(0.32–0.46)		0.45(0.37–0.54)	
2001			0.36(0.30–0.44)		0.44(0.36–0.53)	
2002			0.38(0.31–0.46)		0.46(0.38–0.56)	

Effect	Model 1		Model 2		Model 3	
	OR(95% CI)	p	OR(95% CI)	p	OR(95% CI)	p
Age at diagnosis		<0.001		<0.001		<0.001
65–69			ref		ref	
70–74			0.98(0.87–1.11)		1.03(0.91–1.16)	
75–79			0.95(0.84–1.09)		1.00(0.87–1.14)	
80+			1.73(1.51–1.98)		1.74(1.51–2.00)	
Married				<0.001		<0.001
No			ref		ref	
Yes			0.78(0.71–0.86)		0.82(0.75–0.90)	
Comorbidity score				0.016		0.063
0			ref		ref	
1			0.87(0.78–0.96)		0.89(0.80–0.98)	
2+			1.01(0.88–1.15)		1.02(0.89–1.17)	
Surgery type				<0.001		<0.001
No surgery			ref		ref	
Exploratory Biopsy			0.84(0.73–0.98)		0.85(0.73–0.99)	
TURP			0.67(0.58–0.78)		0.63(0.54–0.73)	
Prostatectomy			5.73(5.01–6.56)		6.51(5.68–7.47)	
Zip code median household income				0.012		0.081
≤$41,302			ref		ref	
$41,303–$51,222			0.86(0.76–0.98)		0.86(0.76–0.98)	
$51,223–$64,833			0.87(0.76–0.98)		0.89(0.78–1.01)	
$64,834–$200,008			0.80(0.70–0.91)		0.85(0.74–0.98)	
n=	18,067		15,781		15,781	
AIC=	19,586		15,136		14,731	

OR odds ratio; *CI* confidence interval; *TURP* transurethral resection of the prostate; *AIC* Akaike information criterion, represents the model goodness of fit, with lower number representing better fit