Geographic Patterns of Prostate Cancer Mortality and Variations in Access to Medical Care in the United States

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Abstract

Background: **Striking geographic variation in prostate cancer death rates have been observed in the United States since at least the 1950s; reasons for these variations are unknown. Here we examine the association between geographic variations in prostate cancer mortality and regional variations in access to medical care, as reflected by the incidence of late-stage disease, prostate-specific antigen (PSA) utilization, and residence in rural counties.**
Methods: **We analyzed mortality data from the National Center for Health Statistics, 1996 to 2000, and incidence data from 30 population-based central cancer registries from the North American Association of Central Cancer Registries, 1995 to 2000. Ecological data on the rate of PSA screening by registry area were obtained from the 2001 Behavioral Risk Factor Surveillance System. Counties were grouped into metro and nonmetro areas according to Beale codes from the Department of Agriculture. Pearson correlation analyses were used to examine associations.**
Results: **Significant correlations were observed between the incidence of late-stage prostate cancer and death rates for Whites (r = 0.38, P = 0.04) and Blacks (r = 0.53, P = 0.03). The variation in late-stage disease corresponded to about 14% of the variation in prostate cancer death rates in White men and 28% in Black men. PSA screening rate was positively associated with total prostate cancer incidence (r = 0.42, P = 0.02) but inversely associated with the incidence of late-stage disease (r = −0.58, P = 0.009) among White men. Nonmetro counties generally had higher death rates and incidence of late-stage disease and lower prevalence of PSA screening (53%) than metro areas (58%), despite lower overall incidence rates.**
Conclusion: **These ecological data suggest that 10% to 30% of the geographic variation in mortality rates may relate to variations in access to medical care.** (Cancer Epidemiol Biomarkers Prev 2005;14(3):590–5)

Introduction

In the United States, the death rate from prostate cancer is highest in the Northwest and North Central states among White men but highest in the South Atlantic states among Black men (1). The reasons for these geographic patterns are unclear, although the racial difference partly reflects the more limited geographic distribution of Black men. Prior studies focused primarily on exposures to agricultural and industrial chemicals and reported association with farming and textile and metal-using industries (2-4). To our knowledge, no study has examined whether access to and utilization of medical care, as reflected by differences in stage at diagnosis, may also contribute to these geographic patterns. Hereafter, we refer access to and utilization of medical care as access to medical care.

Until recently, the opportunity to study geographic variability in stage at diagnosis using population-based cancer registries in the United States has been limited to registries in the Surveillance Epidemiology and End Results program (nine geographic areas), covering about 10% of the U.S. population. Since the early 1990s, many other population-based cancer registries have been created or expanded through the National Program of Cancer Registries; these data, available through the North American Association of Central Cancer Registries, provide information on cancer incidence rates and stage of diagnosis for as much as 68% of the United States. Herein, we examine whether geographic patterns of prostate cancer death rates are related to variations in distant-stage disease, an indirect measure of variations in medical care. In 1995, distant-stage prostate cancer comprised about 6% of incident cases but contributed over 25% of prostate cancer deaths among U.S. White men (5). A 5-year relative survival for men diagnosed with distant-stage disease was 34% compared with 100% for local and regional and 88% for unstaged disease (6). We examined the relationship of stage at diagnosis, utilization of prostate-specific antigen (PSA) screening, and degree of urbanization/population density to prostate cancer incidence and death rates in 30 population-based U.S. cancer registries.

Materials and Methods

We obtained mortality data from the National Center for Health Statistics and incidence data from the North American Association of Central Cancer Registries for 30 geographic areas (28 states, the District of Columbia, and Atlanta), representing about 40% of the U.S. population (7). Criteria for inclusion of cancer registries in the study were completeness of reporting, duplicative records not exceeding 0.2%, internal consistency among data items, <5% unknown in critical data fields, <5% of all cases registered with information only from death certificates, and agreement by the registries to participate (7). All registries agreed to participate.

We computed average annual prostate cancer incidence rates in men ages ≥40 years for 1995 to 2000 for each cancer

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registry by race (Whites and Blacks) and stage at diagnosis according to Surveillance Epidemiology and End Results Summary Stage 1977 (all stages, local/regional, distant, and unstaged; refs. 8, 9). We also computed average annual prostate cancer death rates for 1996 to 2000 for the corresponding demographic groups and geographic areas. All rates were age adjusted to the year 2000 U.S. population standard and expressed per 100,000 men.

Data on the rate of PSA utilization within the last year among men ages ≥50 years with no history of prostate cancer by state were abstracted from published data (10), derived from the 2001 Behavioral Risk Factor Surveillance System, an annual cross-sectional, population-based, random-digit-dialed telephone survey given by the Centers for Disease Control and Prevention for tracking health care use and risk behaviors at a state level. Using the Beale Codes from the U.S. Department of Agriculture (11), we calculated incidence and death rates by degree of urbanization/population density and tested for differences in rates between metro and nonmetro areas by assuming a Poisson distribution (12). The analyses by county using Beale Codes could not control for covariates other than age and race, due to lack of county identifier.

We measured the association between geographic variations in prostate cancer death rates and incidence rates of distant-stage disease for Whites and for Blacks using Pearson correlations (13). We then estimated the proportion of variability in the death rates explained by the association with the incidence rates by squaring the correlation coefficient. We also assessed the geographic correlations between death rates and overall incidence rates, between PSA screening rate and overall incidence, and between incidence of distant-stage disease and PSA screening rate. All variables used in the Pearson correlation analyses satisfied the bivariate normality assumption. The correlations of the percentage of population residing in nonmetro areas with prostate cancer incidence and death rates were measured as partial correlation (13). Rates based on <25 cases or deaths were excluded from the analyses. Therefore, the analyses for Whites were based on 29 cancer registries (28 states and Atlanta); the analyses for Black men were based on 17 cancer registries (15 states, the District of Columbia, and Atlanta). Correlation analyses pertaining to PSA screening rate were restricted to Whites because of lack of reliable PSA rate estimates among Black men for many states.

Results

The geographic variation in prostate cancer incidence, mortality, and PSA screening is shown in Table 1. Among White men, ages ≥40 years, the age-adjusted prostate cancer death rate (per 100, 000 men per year) ranged from 60.8 in Alaska to 86.4 in Wyoming. The incidence rate for all stages combined ranged from 294.8 in Arizona to 427.8 in New Jersey; the incidence rate of distant-stage disease ranged from 10.4 in Atlanta to 28.6 in Hawaii. Among Black men, ages ≥40 years, the corresponding range in rates (per 100,000 per year) was from 129.2 in Rhode Island to 196.7 in North Carolina for mortality, from 374.8 in Hawaii to 692.6 in Michigan for overall incidence, and from 33.3 in Arizona to 76.9 in West Virginia for incidence of distant-stage disease. Rates for unstaged disease also varied widely across cancer registries in both White and Black men.

No correlation was seen between prostate cancer death rates and overall incidence rates across states among either White men ($r = 0.17$, $P = 0.39$) or Black men ($r = -0.30$, $P = 0.23$). In contrast, prostate cancer death rates were directly correlated with incidence rates of distant-stage disease for both White men ($r = 0.38$, $P = 0.04$) and Black men ($r = 0.53$, $P = 0.03$; Fig. 1). The variation in late-stage disease could account for 14% of the geographic variation in prostate cancer mortality in White and 28% in Black men. Geographic variations in PSA screening rate among White men correlated directly with overall incidence rates ($r = 0.42$, $P = 0.02$) but inversely with incidence rates of distant-stage disease ($r = -0.58$, $P < 0.0001$; Fig. 2).

Prostate cancer death rates and rates of distant-stage disease were higher in nonmetro than metro areas despite lower overall incidence rates (Table 2). On average, the death rate in nonmetro areas compared with metro areas was 12% higher in Black men and 4% higher in White men. Similarly, the incidence rates of distant-stage disease were 13% higher in Whites and 9% higher in Blacks in nonmetro than in metro areas. Furthermore, the incidence of unstaged disease was 2% higher in Whites and 15% higher in Blacks in nonmetro than in metro areas. The association between prostate cancer death rates and rates of distant-stage disease became substantially weaker when adjusted for differences in the percentage of the population residing in nonmetro areas (White men: $r = 0.24$, $P = 0.21$; Black men: $r = 0.31$, $P = 0.24$) but changed minimally when adjusted for the incidence of unstaged disease in either White men ($r = 0.33$, $P = 0.09$) or Black men ($r = 0.56$, $P = 0.02$).

Discussion

Our principal findings are that the geographic variation in prostate cancer death rates is positively associated with incidence of late-stage disease and with residence in nonmetro areas and that the incidence of late-stage disease is inversely associated with the utilization of PSA testing. All of these factors suggest that lower access to medical care may contribute to a higher death rate from prostate cancer in certain regions of the United States. In our analyses, geographic variations in late-stage disease may account for about 14% of the geographic variation of mortality in White men and 28% in Black men.

Other factors that may contribute to the geographic variation in prostate cancer mortality involve regional variations in underlying risk factors or exposures that reduce risk. Farming has been consistently associated with increased risk of prostate cancer (3, 14-19). Dosemeci et al. (3) estimated that occupations related to farming could account for about 38% of the excess prostate cancer death rates in the southeastern United States among Black men. Based on a limited study, however, farm-related occupations at county level did not account for the excess regional risk in death rates from prostate cancer among Whites (4). Historically, elevated rates of prostate cancer mortality in the Northeast and North Central regions of the United States have been associated with exposures from textile and machinery industries (2), although the extent to which these occupations influence state or regional rates is unclear. More recently, mortality from prostate cancer has been associated with obesity in case control and prospective epidemiologic studies (20-22); however, correlation in geographic variations between obesity and mortality has not been established.

Another factor that varies by region and that has been proposed to protect against prostate cancer is UV radiation from sun exposure. Sunlight triggers the synthesis of vitamin D, which has been hypothesized to reduce the risk of prostate cancer (23). However, findings from analytic studies have been inconsistent on the role of vitamin D in the development of prostate cancer (24-30).

A strength of our study is that data are based on a much larger geographic area than could be evaluated in the past. Stage at diagnosis is a strong predictor of prognosis and an

Table 1. Prostate cancer death rates, incidence rates (overall and stage specific), and PSA testing for selected U.S. cancer registries, men ages ≥40 years

	White					Black				
		Incidence					Incidence			
Cancer registry/state	Death rate	All cases rate	Local and regional rate	Distant rate	Unstaged rate	Recent PSA test (%), age >50, 2001*	Death rate	All cases rate	Local and regional rate	Distant rate	Unstaged rate	Recent PSA test (%), age >50, 2001*
Alaska	60.8	401.3	258.2	15.5	127.7	62.3	†	653.0	457.7	†	†	†
Arizona	67.5	294.8	215.9	11.8	67.1	62.0	154.8	385.8	255.9	33.3	96.7	†
Colorado	71.2	367.6	274.4	18.4	74.8	60.4	172.6	476.4	363.4	39.6	73.4	†
Connecticut	67.9	377.6	332.4	18.2	27.1	60.6	167.6	590.0	500.5	46.0	43.6	64.4
District of Columbia	67.2	373.8	320.5	†	41.2	58.5	164.2	663.7	516.2	47.3	100.2	56.8
Atlanta	72.4	385.2	311.4	10.4	63.4	71.7	169.9	614.2	481.5	48.7	84.0	56.9
Hawaii	75.6	367.5	315.3	28.6	23.6	45.6	†	374.8	351.8	†	†	†
Idaho	82.1	368.1	283.9	20.5	63.7	52.5	†	†	†	†	†	†
Illinois	73.7	337.0	278.7	19.6	38.6	52.5	167.4	535.5	386.5	58.7	90.3	62.5
Iowa	75.2	349.0	297.1	23.3	28.6	52.1	180.3	605.9	485.2	†	†	†
Kentucky	77.1	300.0	220.0	20.6	59.4	52.8	155.2	465.9	317.4	46.3	102.2	51.1
Louisiana	73.0	359.9	302.0	18.0	39.9	57.0	164.4	516.2	381.8	56.8	77.6	46.2
Maine	75.1	339.1	296.2	24.2	18.7	48.1	†	†	†	†	†	†
Massachusetts	75.9	402.7	353.8	17.0	31.8	63.0	142.9	568.3	487.6	36.0	44.7	41.5
Michigan	73.9	397.7	320.1	14.8	62.9	62.6	153.7	692.6	561.9	42.7	87.9	47.3
Montana	81.3	370.3	278.1	18.3	73.9	57.4	†	†	†	†	†	†
Nebraska	67.8	361.9	308.7	20.4	32.8	48.4	142.5	493.0	389.7	†	†	†
New Hampshire	75.8	331.3	287.3	18.1	25.9	56.0	†	†	†	†	†	†
New Jersey	72.3	427.8	330.1	17.0	80.8	65.1	167.2	657.3	494.8	57.4	105.2	63.7
North Carolina	72.7	312.0	271.2	14.3	26.5	55.5	196.7	501.0	380.7	56.5	63.8	47.4
North Dakota	81.7	413.1	357.4	16.6	39.1	55.4	†	†	†	†	†	†
Oregon	80.3	356.1	298.9	17.8	39.4	53.5	177.3	500.7	384.6	†	†	†
Pennsylvania	73.9	362.4	296.6	17.6	48.2	63.9	172.7	610.6	483.1	47.5	80.0	†
Rhode Island	77.7	402.8	266.8	19.2	116.8	62.7	129.2	465.2	309.3	†	109.9	†
South Carolina	72.3	343.6	286.9	13.9	42.8	61.1	195.9	601.1	454.6	55.9	90.6	51.1
Utah	83.8	406.4	385.8	17.9	2.7	52.6	†	535.9	475.8	†	†	†
Washington	70.6	380.4	298.8	18.1	63.6	52.3	146.6	546.9	421.2	40.2	85.4	†
West Virginia	72.3	325.1	250.7	22.0	52.5	58.1	170.1	556.8	400.8	76.9	79.0	†
Wisconsin	80.0	365.6	318.2	21.4	25.9	54.5	145.1	595.2	511.6	48.9	34.8	†
Wyoming	86.4	408.2	279.0	18.6	110.6	64.1	†	†	†	†	†	†

NOTE: Death rates are for 1996 to 2000 and incidence rates are for 1995 to 2000. Rates are expressed per 100,000 men and are standardized to the U.S. 2000 population.
* PSA test in the preceding year in men ages ≥50 years with no history of prostate cancer based on 2001 Behavioral Risk Factor Surveillance System Data (7).
† Statistics could not be calculated for incidence and death rates because there were <25 cases or deaths and for PSA testing because there were ≤20 respondents in the survey.

indirect measure of access to medical care (31-33), although it may also reflect other factors. Our findings are not influenced by the choice of correlation method or exclusion of apparent outliers. We presented the association result based on the Pearson correlations because all the variables used in the analyses satisfied the bivariate normal distributions assumptions for Pearson correlation. However, analyses by Spearman correlation provided generally similar results. The relationship between variations in death rates and distant-stage disease became slightly stronger ($r = 0.58$, $P = 0.03$) in Blacks when North Carolina, South Carolina, and West Virginia were excluded as outliers.

Certain limitations of our study may affect interpretations of the results. The analyses are ecological and are not based on individual data except for stage at diagnosis in relation to incidence. The use of state data rather than smaller geographic unit limits the heterogeneity of units within analyses. The heterogeneity and statistical power of our analyses is also constrained by the number of cancer registries that could be included (29 for White men and 17 for Black men). All of these limitations would tend to attenuate the association between the incidence rate of late-stage disease and prostate cancer mortality and would cause our findings to underestimate the true association.

Stage at diagnosis has been interpreted as an indirect measure of access to health care in some previous studies (31-33). We chose to study the incidence rate of prostate cancer diagnosed at distant-stage disease (per 100,000) instead of the percentage of cases diagnosed at later stage because incidence is less influenced by screen detected prostate cancers in the denominator. It is possible that an unmeasured underlying risk factor, such as farming, could affect the case mix of prostate cancer in rural areas by increasing the occurrence of more aggressive disease. If this were the case, the incidence rate of distant-stage disease might reflect exposure to an etiologic agent rather than variations in access to medical care. However, the proportion of poorly differentiated or undifferentiated cases of distant stage was not higher in nonmetro than metro areas in either White men (43% in nonmetro and 45% in metro) or Black men (39% in nonmetro and 44% in nonmetro). Thus, our study found no evidence of differences in case mix associated with degree of urbanization.

We confined our analyses of both incidence and mortality to a 5- or 6-year interval, from 1995 to 2000 for incidence and 1996 to 2000 for mortality because of the lack of incidence data for much of the country before 1995. Because the median survival of late-stage prostate cancer is about 2 years (34), we recognize that some of men who died from late-stage disease in the period of 1996 to 2000 would have been diagnosed before 1995. However, based on data from the nine Surveillance Epidemiology and End Results areas, the geographic pattern of distant-stage disease for 1995 to 2000 was strongly correlated ($r = 0.63$, $P = 0.05$) with the pattern for 1990 to 1995. Hence, our findings on the relationship between late-stage disease and prostate cancer death rates were unlikely to be influenced by lack of historical data. However, the lack of historical data may be more problematic

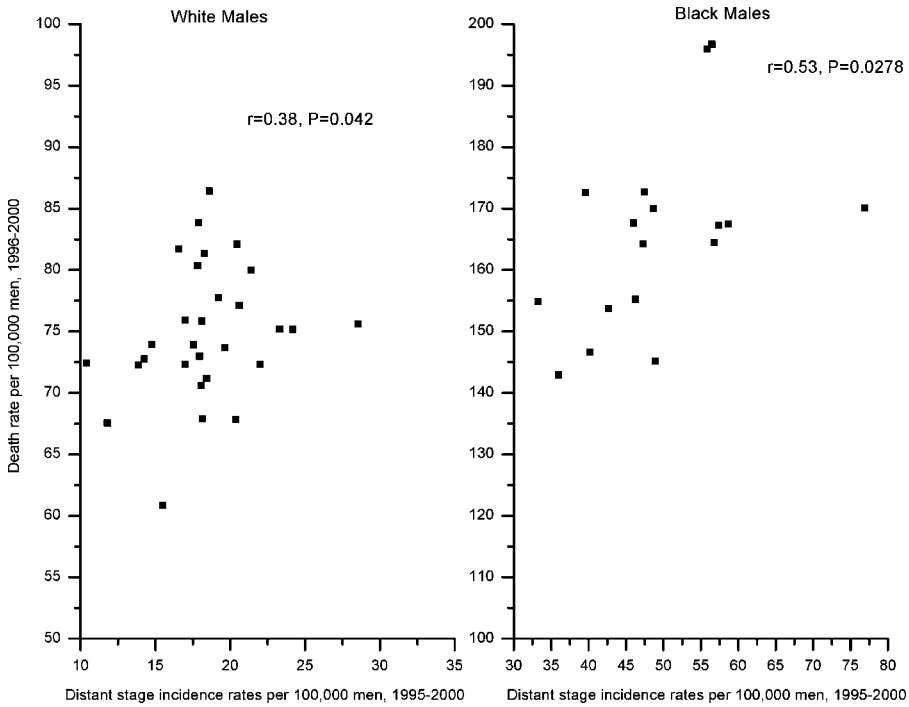

Figure 1. Relationship between the incidence of distant stage disease and death rates from prostate cancer among men age ≥40 years in states included in the analyses. Based on 28 states and one metropolitan area for White men and 15 states and two metropolitan areas for Black men.

for the relationship between overall incidence rate and prostate cancer death rates in which the time lag between diagnosis and death is more protracted.

The variations in incidence of unstaged disease across cancer registries may in part be related to lack of standardized procedures for staging of prostate cancer cases with unknown lymph node status because such cases could be classified differently as either localized/regional or unknown. Unstaged prostate cancer rates were also slightly higher in nonmetro than metro areas, particularly among Blacks. Other researchers have reported similar rural-urban differences in unstaged cases for a number of cancers including prostate cancer in Georgia; these patterns were thought to reflect less rigorous diagnostic evaluation and/or more incomplete medical record documentation in the rural medical facilities (33). The less rigorous diagnostic evaluation in rural areas may be associated with greater comorbid diseases and might reflect further differences in access to medical care. However, adjusting for variation in unstaged incidence across registries did not affect the relationship we observed between prostate cancer death rates and rates of distant-stage disease in either White or Black men.

Table 2. Prostate cancer death and incidence rates in men ages ≥40 years by degree of urbanization, 1995-2000

Degree of urbanization/population size	White incidence rate*					Black incidence rate*				
	Death rate	Overall	Local and regional	Distant	Unstaged	Death rate	Overall	Local and regional	Distant	Unstaged
Metro counties	**71.7**	**368.9**	**303.4**	**17.1**	**48.5**	**166.8**	**586.7**	**455.0**	**51.3**	**80.4**
Central county metro area ≥1 million population	71.2	379.9	312.6	17.0	50.4	164.1	602.9	469.2	50.8	82.9
Fringe county Metro Area GE 1 million pop	74.4	341.9	283.8	17.6	40.5	145.4	498.1	397.7	46.1	54.3
County metro area 250,000-1 million population	72.1	358.1	294.8	16.8	46.5	169.9	557.0	427.0	50.4	79.6
County metro area <250,000 population	72.2	360.1	293.8	18.0	48.3	185.9	541.5	416.6	60.8	64.0
Nonmetro counties	**74.9**	**342.1**	**273.2**	**19.3**	**49.6**	**186.2**	**520.6**	**371.9**	**56.2**	**92.5**
Urban population ≥20,000, adjacent metro area	73.2	344.1	282.5	18.0	43.6	180.6	544.0	416.6	61.0	66.4
Urban population ≥20,000, not adjacent metro area	73.8	372.2	306.3	19.8	46.1	146.7	552.7	425.1	53.0	74.6
Urban population 2,500-19,999, adjacent metro area	75.3	331.4	267.3	18.4	45.7	196.7	512.1	356.6	55.2	100.4
Urban population 2,500-19,999, not adjacent metro area	75.7	347.1	269.5	20.2	57.5	177.5	512.6	358.5	57.0	97.1
Rural or <2,500 urban population, adjacent metro area	78.6	313.8	239.0	20.1	54.7	186.5	471.3	332.7	41.2	97.5
Rural or <2,500 urban population, not adjacent metro area	75.5	330.8	257.5	20.9	52.4	195.8	530.8	323.2	66.0	141.5
Rate ratio (nonmetro to metro counties)	1.04 †	0.93 †	0.90 †	1.13 †	1.02	1.12 †	0.89 †	0.82 †	1.09 †	1.15 †

NOTE: Rates are per 100,000 and are adjusted to the 2000 U.S. population standard.
* Cases were staged according to SEER Summary Stage 1977 (8, 9).
† Rate ratios were statistically significant ($P < 0.05$).

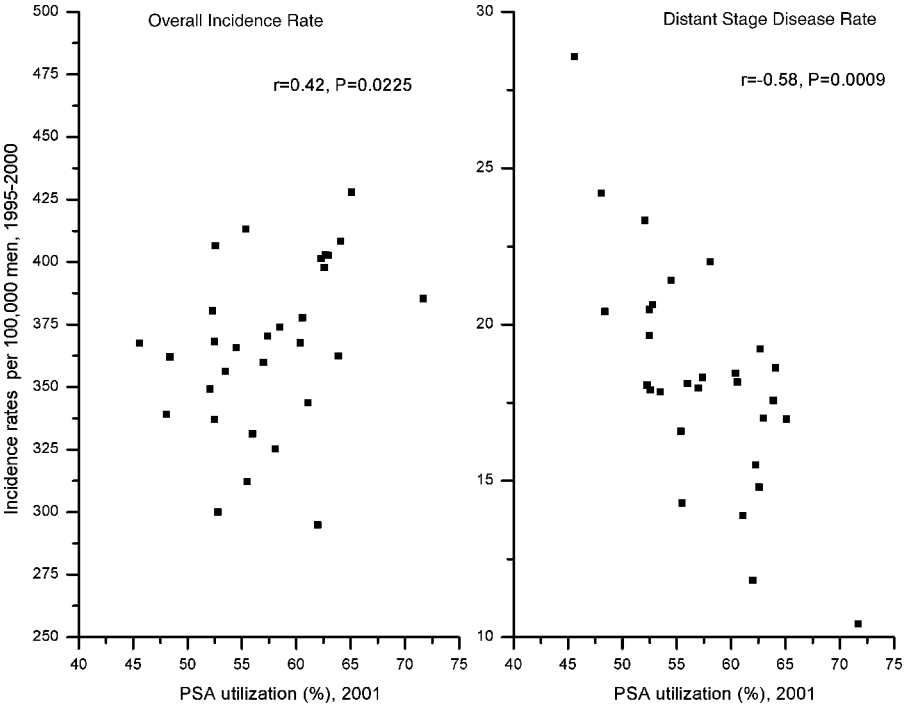

Figure 2. Relationship of PSA utilization to the overall incidence of prostate cancer and to the incidence of distant-stage disease among White men in selected states.

We correlated incidence rates for 1995 to 2000 with self-reported PSA utilization in 2001 because every state included questions about prostate cancer screening in the Behavioral Risk Factor Surveillance System survey for the first time in 2001. Limitations of data from the Centers for Disease Control and Prevention's Behavioral Risk Factor Surveillance System have been discussed in detail elsewhere (35). Briefly, the response rates widely vary across states and the survey relies exclusively on telephone interviews. Although men with a history of prostate cancer who receives PSA testing for follow-up were excluded, the survey cannot distinguish between tests conducted for screening from those for diagnostic purposes and may overestimate the actual utilization rates (36, 37). Despite these methodologic limitations, PSA utilization rates positively correlated with overall incidence rates and inversely correlated with incidence rates of distant-stage disease.

In conclusion, our data suggest that variations in medical care should be considered in future studies of the geographic variation in prostate cancer mortality.

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