

## Time Trends and Local Variation in Primary Treatment of Localized Prostate Cancer

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### ABSTRACT

#### Purpose

In the absence of high-level evidence or clinical guidelines supporting any given active treatment approach over another for localized prostate cancer, clinician and patient preferences may lead to substantial variation in treatment use.

#### Methods

Data were analyzed from 36 clinical sites that contributed data to the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry. Distribution of primary treatment use was measured over time. Prostate cancer risk was assessed using the D'Amico risk groups and the Cancer of the Prostate Risk Assessment (CAPRA) score. Descriptive analyses were performed, and a hierarchical model was constructed that controlled for year of diagnosis, cancer risk variables, and other patient factors to estimate the proportion of variation in primary treatment selection explicable by practice site.

#### Results

Among 11,892 men analyzed, 6.8% elected surveillance, 49.9% prostatectomy, 11.6% external-beam radiation, 13.3% brachytherapy, 4.0% cryoablation, and 14.4% androgen deprivation monotherapy. Prostate cancer risk drives treatment selection, but the data suggest both overtreatment of low-risk disease and undertreatment of high-risk disease. The former trend appears to be improving over time, while the latter is worsening. Treatment varies with age, comorbidity, and socioeconomic status. However, treatment patterns vary markedly across clinical sites, and this variation is not explained by case-mix variability or known patient factors. Practice site explains a proportion of this variation ranging from 13% for androgen deprivation monotherapy to 74% for cryoablation.

#### Conclusion

Substantial variation exists in management of localized prostate cancer that is not explained by measurable factors. A critical need exists for high-quality comparative effectiveness research in localized prostate cancer to help guide treatment decision making.

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### INTRODUCTION

An estimated 192,280 men will be diagnosed with prostate cancer this year and will face a complex decision with respect to timing of and type of initial management.<sup>1</sup> Prostate cancer is second only to lung cancer as a cause of cancer mortality among men in the United States,<sup>1</sup> but the natural history of the disease is variable and is frequently indolent, even in the setting of expectant management.<sup>2</sup> The choice of any available treatment, moreover, is associated with risks of adverse effects and substantial impacts on health-related quality of life.<sup>3</sup>

No contemporary clinical trials randomly assigning men among any of the major active treatment modalities—radical prostatectomy, interstitial or external-beam radiation therapy, or androgen deprivation therapy—have been reported. Indeed, a

recent systematic review commissioned by the Agency for Healthcare Research and Quality found that insufficient evidence exists to conclude that there is greater benefit for any given treatment approach over another.<sup>4</sup> The recently updated clinical practice guideline published by the American Urological Association (AUA) endorses alternatives for localized disease, including active surveillance, prostatectomy, and radiation therapy (interstitial or external-beam), but again was unable to draw conclusions regarding the relative benefits of these alternatives.<sup>5</sup>

In the absence of high-quality evidence regarding the comparative effectiveness of these alternatives, clinician and patient preferences and values play a significant role in determining treatment approach<sup>6</sup>; along with various financial, legal, and other incentives, these preferences tend to lead to

**Table 1.** Sociodemographic and Clinical Characteristics of Men by Primary Treatment Group

Characteristic	WW/AS		RP		Brachytherapy		EBRT		Cryotherapy		PADT		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<b>Age, years</b>														
< 50	4	1.3	276	88.2	15	4.8	6	1.9	1	0.3	11	3.5	313	2.6
50-65	130	2.5	3,813	73.6	520	10.0	288	5.6	146	2.8	285	5.5	5,182	43.6
65-75	345	7.4	1,796	38.6	801	17.2	751	16.1	273	5.9	686	14.7	4,652	39.1
> 75	331	19.0	46	2.6	247	14.2	337	19.3	54	3.1	730	41.8	1,745	14.7
<b>Race</b>														
White	710	6.9	5,191	50.7	1,394	13.6	1,142	11.1	436	4.3	1,373	13.4	10,246	86.2
African American	76	6.2	548	44.5	118	9.6	202	16.4	27	2.2	260	21.1	1,231	10.4
Latino	9	4.7	79	41.1	53	27.6	18	9.4	6	3.1	27	14.1	192	1.6
Asian	8	8.6	36	38.7	11	11.8	11	11.8	1	1.1	26	28.0	93	0.8
Native American	0	0.0	19	76.0	0	0.0	1	4.0	2	8.0	3	12.0	25	0.2
Mixed	2	4.4	27	60.0	6	13.3	2	4.4	2	4.4	6	13.3	45	0.4
Unknown	5	8.3	31	51.7	1	1.7	6	10.0	0	0.0	17	28.3	60	0.5
<b>Region</b>														
West	227	13.1	829	47.8	202	11.7	130	7.5	66	3.8	279	16.1	1,733	14.6
East	303	5.7	2,785	51.9	631	11.8	772	14.4	304	5.7	566	10.6	5,361	45.1
Midwest	160	6.3	1,450	57.2	296	11.7	227	9.0	47	1.9	356	14.0	2,536	21.3
South	120	5.3	867	38.3	454	20.1	253	11.2	57	2.5	511	22.6	2,262	19.0
<b>Insurance</b>														
Private	140	2.8	3,565	70.4	592	11.7	255	5.0	165	3.3	347	6.9	5,064	42.6
Medicare	157	9.2	501	29.2	255	14.9	333	19.4	106	6.2	361	21.1	1,713	14.4
Medicare + supplemental insurance	414	9.8	1,501	35.7	650	15.5	650	15.5	189	4.5	802	19.1	4,206	35.4
Veterans affairs	58	17.7	135	41.3	52	15.9	27	8.3	0	0.0	55	16.8	327	2.7
Other/unknown	41	7.0	229	39.3	34	5.8	117	20.1	14	2.4	147	25.3	582	4.9
<b>Education</b>														
No high school	38	7.4	166	32.1	79	15.3	85	16.4	20	3.9	129	25.0	517	4.3
Some high school	98	10.6	345	37.2	138	14.9	123	13.3	42	4.5	182	19.6	928	7.8
High school graduate	169	7.2	1,130	48.0	311	13.2	293	12.4	125	5.3	327	13.9	2,355	19.8
Some college	126	7.1	936	52.8	221	12.5	177	10.0	77	4.3	235	13.3	1,772	14.9
College graduate	83	5.0	993	59.9	167	10.1	186	11.2	73	4.4	155	9.4	1,657	13.9
Graduate school	93	5.2	1,084	60.2	225	12.5	186	10.3	42	2.3	170	9.4	1,800	15.1
Missing	203	7.1	1,277	44.6	442	15.4	332	11.6	95	3.3	514	18.0	2,863	24.1
<b>Annual income, \$</b>														
Zero	1	2.7	10	27.0	6	16.2	5	13.5	2	5.4	13	35.1	37	0.3
< 5,000	5	6.0	17	20.2	9	10.7	17	20.2	4	4.8	32	38.1	84	0.7
5,000-10,000	19	6.8	89	31.9	31	11.1	39	14.0	11	3.9	90	32.3	279	2.3
10,000-20,000	98	10.9	269	29.8	156	17.3	146	16.2	48	5.3	185	20.5	902	7.6
20,000-30,000	111	8.5	532	40.8	196	15.0	194	14.9	67	5.1	205	15.7	1,305	11.0
30,000-50,000	134	6.8	1,000	50.4	264	13.3	231	11.6	101	5.1	254	12.8	1,984	16.7
50,000-75,000	64	4.4	904	62.5	156	10.8	121	8.4	55	3.8	147	10.2	1,447	12.2
> 75,000	80	4.1	1,396	71.0	188	9.6	147	7.5	45	2.3	110	5.6	1,966	16.5
Unknown	298	7.7	1,714	44.1	577	14.8	482	12.4	141	3.6	676	17.4	3,888	32.7
<b>Comorbidities</b>														
0	72	4.4	1,059	65.5	145	9.0	147	9.1	54	3.3	141	8.7	1,618	13.6
1	117	4.8	1,453	59.3	283	11.5	254	10.4	114	4.6	231	9.4	2,452	20.6
2	154	6.6	1,158	49.7	317	13.6	285	12.2	102	4.4	312	13.4	2,328	19.6
3	137	8.9	645	41.8	225	14.6	188	12.2	72	4.7	275	17.8	1,542	13.0
> 3	137	11.2	399	32.6	179	14.6	204	16.7	47	3.8	258	21.1	1,224	10.3
Unknown	193	7.1	1,217	44.6	434	15.9	304	11.1	85	3.1	495	18.1	2,728	22.9
<b>Risk group</b>														
Low	397	9.2	2,449	56.8	691	16.0	315	7.3	132	3.1	330	7.6	4,314	36.3
Intermediate	209	4.8	2,283	52.9	581	13.5	530	12.3	194	4.5	515	11.9	4,312	36.3
High	58	3.2	576	32.2	135	7.5	324	18.1	109	6.1	588	32.8	1,790	15.1
Unknown	146	9.9	623	42.2	176	11.9	213	14.4	39	2.6	279	18.9	1,476	12.4
<b>CAPRA score</b>														
0-2	358	7.4	2,845	58.9	810	16.8	315	6.5	153	3.2	352	7.3	4,833	40.6
3-5	166	4.8	1,720	49.7	453	13.1	465	13.4	167	4.8	487	14.1	3,458	29.1
6-10	33	2.6	338	26.6	109	8.6	272	21.4	74	5.8	445	35.0	1,271	10.7
Unknown	253	10.9	1,028	44.1	211	9.1	330	14.2	80	3.4	428	18.4	2,330	19.6
<b>Total</b>	<b>810</b>		<b>5,931</b>		<b>1,583</b>		<b>1,382</b>		<b>474</b>		<b>1,712</b>		<b>11,892</b>	

Abbreviations: WW/AS, watchful waiting/active surveillance; RP, radical prostatectomy; EBRT, external-beam radiation therapy; PADT, primary androgen deprivation therapy; CAPRA, Cancer of the Prostate Risk Assessment.

unwarranted variation in approaches to care across health care regions or localities.<sup>7</sup> Indeed, previous studies have identified substantial local and regional variation in the use of radical prostatectomy and androgen deprivation therapy, but they were based on older data and were unable to adjust adequately for prostate cancer risk characteristics.<sup>8,9</sup> We analyzed a large national registry of men with localized prostate cancer to determine trends over time in treatment of cancers at varying levels of progression risk, and to characterize and quantify variation in primary treatment at the level of the clinical practice site.

## METHODS

Data were reviewed from the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE), a national disease registry of men with biopsy-proven prostate adenocarcinoma. CaPSURE participants were accrued from 40 urology practices across the United States, of which three were academic and the remainder were community-based. Participating urologists consecutively recruited newly diagnosed men and reported initial and follow-up clinical data, including staging tests and treatments. Patients were treated per their clinicians' usual practices and were followed until time of death or withdrawal from the study. All patients provided written, informed consent under local and central institutional review board supervision. Details regarding CaPSURE's methodology have been reported previously.<sup>10,11</sup>

As of July 2008, there were 13,805 men enrolled in CaPSURE. Of these, 534 had advanced (clinical stage > T3aN0M0) disease at time of diagnosis and were excluded, as were 421 diagnosed before 1990. A total of 44 patients were treated at one of four practice sites contributing fewer than 30 patients each to the data set and were excluded. Finally, 914 men managed with a primary treatment other than radical prostatectomy, external-beam radiation therapy, brachytherapy, cryoablation, watchful waiting/active surveillance (CaPSURE does not distinguish these two terms), or primary androgen deprivation therapy, or whose primary treatment was unknown, were excluded. Thus, the analytic data set comprised 11,892 men managed at 36 practice sites.

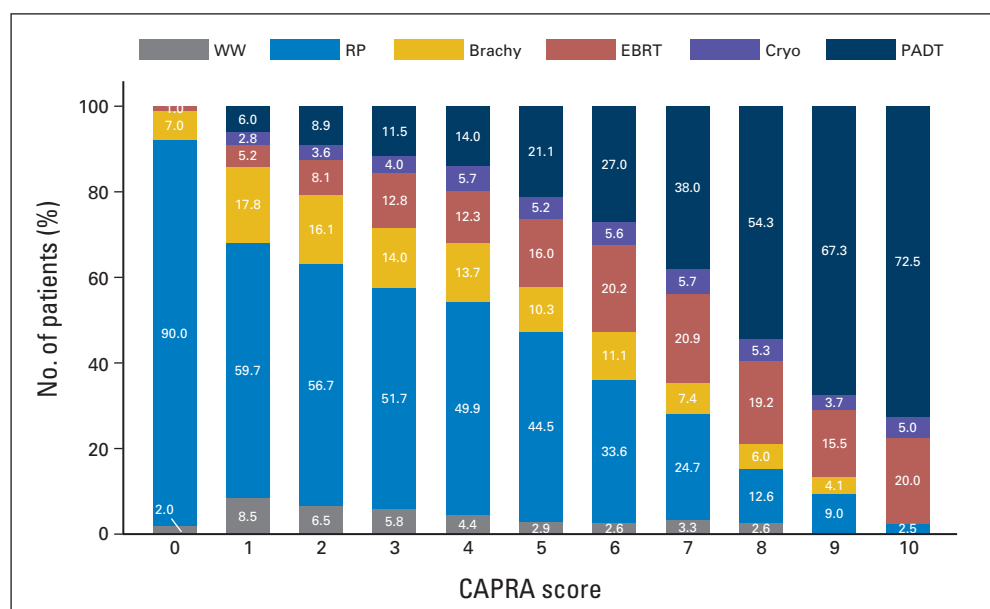
Sociodemographic variables, including age, race, geographic region, insurance type, education, and household income, were recorded and compared across primary treatments, and comorbidity was assessed as previously described.<sup>12</sup> Significance of differences across treatments was assessed with the  $\chi^2$  test for categorical variables and the Mantel-Haenszel  $\chi^2$  test for ordinal and

categorized continuous variables. Prostate cancer risk was summarized using the D'Amico classification, which stratifies men to low, intermediate, and high risk based on the prostate-specific antigen (PSA), Gleason score, and clinical T stage as endorsed by the AUA guideline<sup>5</sup>; and the University of California, San Francisco (UCSF) Cancer of the Prostate Risk Assessment (CAPRA) score, which is a 0 to 10 multivariable score with improved accuracy compared with the risk groups, derived from the same variables with the addition of age and percent of positive biopsy cores. The CAPRA score has also been validated as a grouped score yielding three strata, with scores of 0 to 2, 3 to 5, and 6 to 10 indicating low, intermediate, and high risk, respectively.<sup>13</sup>

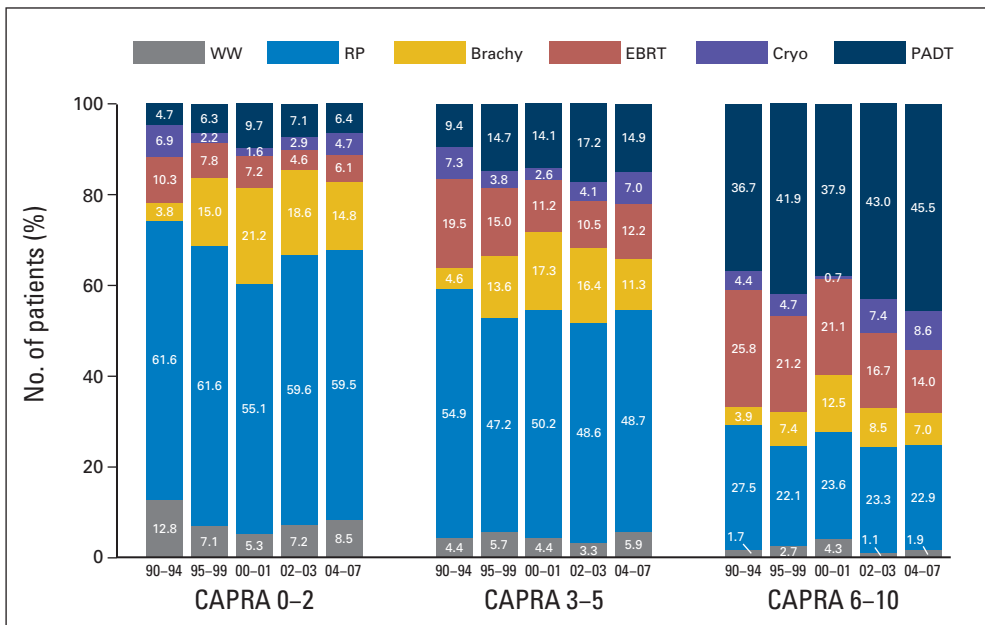
Treatment distributions were examined for patients at each individual CAPRA score level, and trends over time were examined for men in each risk stratum as defined by grouped CAPRA scores. These trends were tested for statistical significance with the Mantel-Haenszel  $\chi^2$  test. Treatment distribution was plotted for each individual practice site, with sites sorted by case-mix in terms of prostate cancer risk as measured by the mean CAPRA score for all patients managed at each site. To estimate the proportion of treatment variation attributable to the practice site, a random effects hierarchical logit model was tested for each primary treatment modality, with adjustment for year of diagnosis, age, race/ethnicity, income, education, geographic region, Charlson score, PSA, Gleason score, clinical T stage, and percent of positive biopsy cores. The intraclass correlation coefficient (ICC) for clinical site was assessed to measure the proportion of treatment variation attributable to practice site. These analyses were repeated on the subset of patients who had low-risk features under the AUA guidelines (PSA < 10 ng/mL, Gleason score  $\leq$  6, and clinical stage  $\leq$  T2a).<sup>5</sup> The ICC was also calculated for use of neoadjuvant androgen deprivation therapy among men undergoing external-beam radiation therapy, and the frequency of neoadjuvant therapy among external-beam radiation patients was compared with the frequency of primary androgen deprivation therapy use across sites by calculation of Pearson's correlation coefficient ( $r$ ). All statistical tests were two-sided, and all analyses were performed using STATA version 10.1 (STATA, College Station, TX).

## RESULTS

Overall, of the 11,892 men in the analytic data set, 810 (6.8%) elected watchful waiting/active surveillance, 5,931 (49.9%) radical prostatectomy, 1,382 (11.6%) external-beam radiation therapy, 1,583 (13.3%)



**Fig 1.** Treatment patterns by risk level. Treatment distribution at each level of risk as measured by the Cancer of the Prostate Risk Assessment (CAPRA) score is illustrated. Treatment trends by risk group were statistically significant by Mantel-Haenszel  $\chi^2$  test,  $P < .001$ . WW, watchful waiting/active surveillance; RP, radical prostatectomy; Brachy, brachytherapy; EBRT, external-beam radiation therapy; Cryo, cryoablation; PADT, primary androgen deprivation therapy.



**Fig 2.** Treatment trends over time by risk group. Changes over time in primary treatment patterns across all practice sites, by risk groups defined by categorized Cancer of the Prostate Risk Assessment (CAPRA) scores. Trends over time for each risk group were statistically significant by Mantel-Haenszel  $\chi^2$  test,  $P < .001$ . WW, watchful waiting; RP, radical prostatectomy; Brachy, brachytherapy; EBRT, external-beam radiation therapy; Cryo, cryoablation; PADT, primary androgen deprivation therapy.

brachytherapy, 474 (4.0%) cryoablation, and 1,712 (14.4%) primary androgen deprivation monotherapy.

Table 1 presents the sociodemographic and clinical characteristics of men in each primary treatment group. In general terms, men undergoing prostatectomy were younger than those receiving other treatments, healthier in terms of comorbidity, more likely to have private insurance, and more likely to have high socioeconomic status. Brachytherapy and cryoablation patients were somewhat older and had lower socioeconomic status and higher comorbidity, followed by external-beam radiation therapy patients, and finally primary androgen deprivation and watchful waiting patients. All differences across treatment modalities were statistically significant ( $P < .001$ ).

Prostate cancer risk was a strong driver of treatment selection, as summarized in Table 1 and Figure 1. With increasing risk as measured by the CAPRA score, proportions of prostatectomy, brachytherapy, and watchful waiting decreased consistently, while the proportion of primary androgen deprivation monotherapy increased substantially. The particularly high proportion of prostatectomy patients in the CAPRA 0 stratum reflects the fact that these patients are by definition relatively young (age  $< 50$  years) as well as low risk in other respects. Use of external-beam radiation and cryoablation rose with risk through the low-risk group (CAPRA 0-2) and was relatively consistent across the intermediate-risk (CAPRA 3 to 5) and high-risk (CAPRA 6-10) groups ( $P < .001$ ).

Treatment trends over time were discordant across risk groups, as presented in Figure 2. For low-risk patients, use of brachytherapy and primary androgen deprivation rose through the 1990s at the expense of prostatectomy and watchful waiting, while in the current decade, these trends appear to be reversing. Among intermediate-risk patients, treatment patterns have been relatively stable since the mid-1990s; for high-risk patients, use of prostatectomy has been relatively stable while use of primary androgen deprivation monotherapy has been rising, apparently at the expense of external-beam radiation therapy in particular.

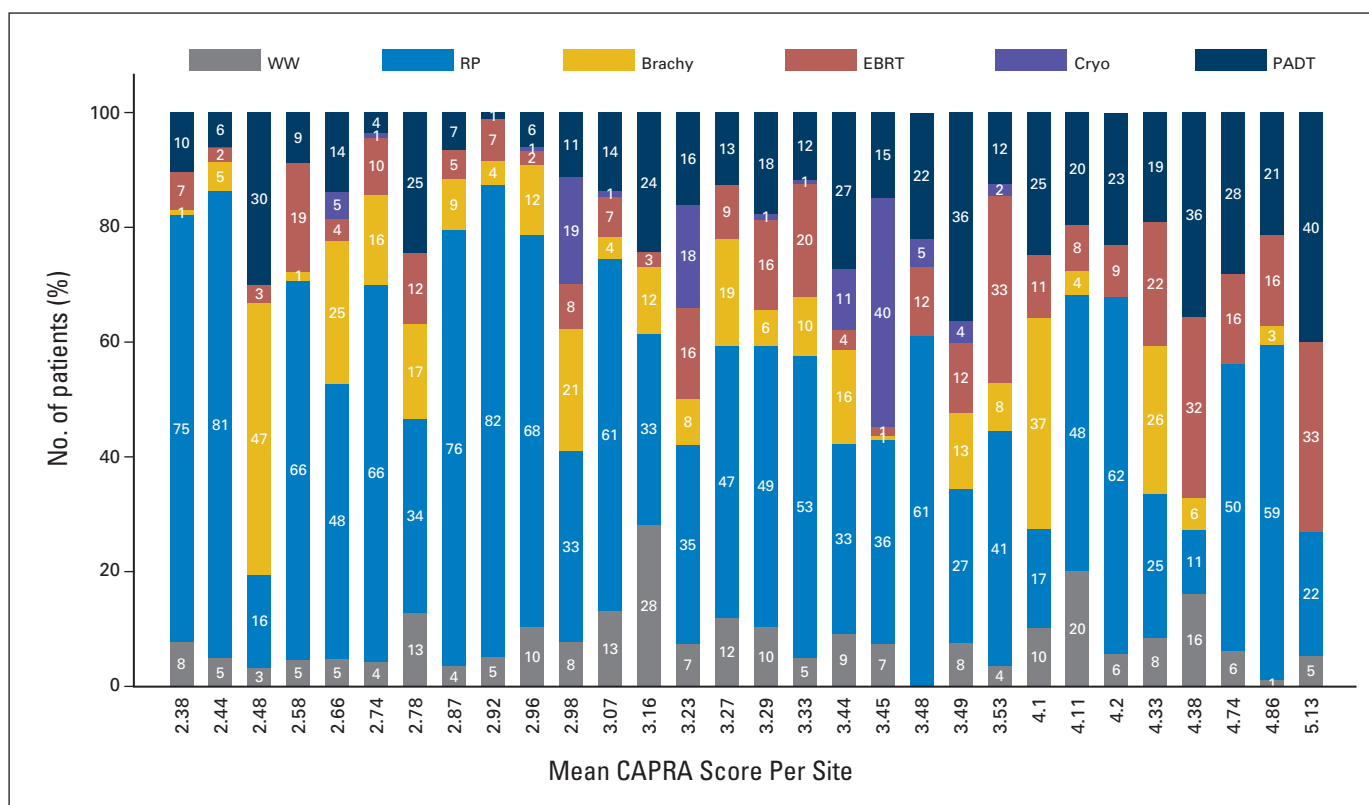
Figure 3 illustrates the substantial variation that exists across practice sites in terms of primary treatment selection for localized

prostate cancer. Use of watchful waiting/active surveillance ranged from 0% to 28% across sites, use of prostatectomy from 11% to 82%, use of brachytherapy from 0% to 47%, use of external-beam radiation therapy from 1% to 33%, use of cryoablation from 0% to 40%, and use of primary androgen deprivation monotherapy from 1% to 40%. The sites in Figure 3 are sorted according to case-mix as assessed by the mean CAPRA score. There is no discernable pattern from left to right (as mean CAPRA score doubles from 2.38 to 5.13) suggesting that the variation in treatment selection across sites was not substantially explained by disease characteristics.

The results of the multivariable analysis are presented in Table 2. Proportion of variation attributable to practice site ranged from 13% for primary androgen deprivation to 74% for cryoablation; among D'Amico low-risk patients only, this proportion ranged from 21% for watchful waiting to 81% for cryoablation. For neoadjuvant androgen deprivation therapy with external-beam radiation, 14% of variation was attributable to practice site. Use of neoadjuvant androgen deprivation therapy correlated modestly with use of primary androgen deprivation at each site ( $r = 0.48$ ;  $P < .001$ ).

## DISCUSSION

In a large, prospectively accrued cohort of men with prostate cancer, disease risk as measured by the CAPRA score does appear to be a major driver of treatment (Fig 1), though the patterns observed are of some concern for both overtreatment of low-risk disease—identified in prior analyses of CaPSURE and other data sources<sup>14,15</sup>—and undertreatment of high-risk localized disease.<sup>16</sup> More men with low-risk disease should be candidates for active surveillance, whereas most with high-risk but clinically localized disease should be offered a chance at cure with multimodal therapy, including either radiation or surgery as the primary local modality.<sup>5</sup> Interestingly, trends over time (Fig 2) suggest that overtreatment of low-risk disease may be ameliorating slightly, whereas potential undertreatment of high-risk disease appears to be a growing concern.



**Fig 3.** Treatment variation among practice sites. Primary treatment distribution from 1990 to 2006 at each clinical site for patients with localized prostate cancer. Sites had at least 30 patients. Clinical sites are arranged in order of increasing average disease risk as assessed by the mean Cancer of the Prostate Risk Assessment (CAPRA) score for that site (listed on x-axis). WW, watchful waiting; RP, radical prostatectomy; Brachy, brachytherapy; EBRT, external-beam radiation therapy; Cryo, cryoablation; PADT, primary androgen deprivation therapy.

Aside from these observed trends over time and risk, this analysis confirms wide variation in practice patterns across clinical sites (Fig 3). Indeed, a substantial proportion of variation in primary treatment selection for localized prostate cancer is attributable to practice site. The degrees of variation observed were similar when the analysis was restricted to men with low-risk disease only. These findings suggest that factors other than cancer risk and patient clinical and sociodemographic factors influence treatment decision making. In fact, treatment of localized prostate cancer is a model of what has been termed

“preference-sensitive” health care, in which patient or clinician preferences, beliefs, or values drive decision making in the absence of strong scientific evidence.<sup>7</sup>

Indeed, clinicians and patients making decisions regarding localized prostate cancer do so in the setting of a relative dearth of high-quality data comparing outcomes following the various available treatments.<sup>4</sup> Only one randomized trial of substantial size and quality has been reported,<sup>17</sup> finding a survival benefit for prostatectomy over watchful waiting; however, the generalizability of the findings to contemporary patients, and to subgroups of various ages and levels of risk, has been the subject of ongoing debate. The Prostate Cancer Intervention Versus Observation Trial (PIVOT) study, also randomly assigning patients to surgery versus watchful waiting, completed accrual; results are expected during 2010.<sup>18</sup>

However, no trials that randomly assign patients among active treatment modalities have yet been completed. The Surgical Prostatectomy Versus Interstitial Radiation Intervention Trial (SPIRIT), intended to compare surgery with brachytherapy, closed because of poor accrual.<sup>19</sup> The Prostate Testing for Cancer and Treatment (ProtecT) study successfully randomized men in the United Kingdom to a three-arm trial comparing prostatectomy, radiation, and surveillance, though results will not be available until the middle of the next decade.<sup>20</sup>

Previous analyses have documented substantial local variation for specific prostate cancer treatments. Using Medicare data from the mid-1990s, for example, the Dartmouth Atlas of Health Care project

**Table 2.** Treatment Variation Attributable to Practice Site

Treatment	$\rho$ (all patients)	95% CI	$\rho$ (low-risk patients only)	95% CI
WW/AS	0.17	0.10 to 0.28	0.21	0.11 to 0.37
RP	0.30	0.20 to 0.42	0.29	0.18 to 0.42
EBRT	0.20	0.12 to 0.31	0.22	0.12 to 0.37
Brachytherapy	0.36	0.23 to 0.52	0.32	0.19 to 0.49
Cryotherapy	0.74	0.56 to 0.87	0.81	0.63 to 0.91
PADT	0.13	0.07 to 0.21	0.23	0.12 to 0.39
NADT	0.14	0.08 to 0.23		

NOTE. Proportion of variation ( $\rho$ ) attributable to practice site is presented with 95% CIs for each primary treatment type, and for NADT given with EBRT.

Abbreviations: WW/AS, watchful waiting/active surveillance; RP, radical prostatectomy; EBRT, external-beam radiation therapy; PADT, primary androgen deprivation therapy; NADT, neoadjuvant androgen deprivation therapy.



analyzed the 10 most commonly performed surgical procedures in the United States, including radical prostatectomy. Findings show that among the 10 procedures, prostatectomy was characterized by the greatest local variation: more than 12-fold greater than the procedure (hip fracture repair) with the least variation and more than eight-fold greater than colectomy for colon cancer. The absolute rates of prostatectomy, adjusted for prevalence of prostate cancer, varied by a factor of nearly 10, from 0.5 to 4.7 per 1,000 Medicare enrollees.<sup>8</sup>

Another recently published study focused on the use of androgen deprivation therapy, based on 1990s data from the Surveillance, Epidemiology, and End Results (SEER)–Medicare linked database. The investigators performed separate analyses for evidence-based androgen deprivation therapy—that is, therapy given together with radiation therapy for high-risk disease (stage T3 or stage T2/poorly differentiated)—and uncertain-benefit therapy, including all other uses. For the evidence-based setting, they found, based on ICC calculations, that disease characteristics accounted for 6.6% of variation, other patient characteristics explained 7.3%, and the treating urologist accounted for 25.4% of variation. For the uncertain benefit setting, the corresponding proportions were 5.3%, 5.0%, and 22.7%. From the early to the late part of the decade, the proportion of variation attributable to the urologist appeared to be increasing.<sup>9</sup>

The major limitation of these studies, aside from the somewhat older data used for analysis, was the lack of adequate cancer risk assessment available in the data sets analyzed: Medicare has no data on risk factors, and the 1990s-era SEER-Medicare data had only stage and differentiation but not PSA levels or Gleason scores. In addition, analyses based on Medicare data by definition are restricted to patients older than age 65 years. The present analysis of treatment variation comprises updated data, including all of the major treatment approaches for localized prostate cancer, and incorporates a robust, well-validated risk assessment score for case-mix adjustment.

The proportions of variation attributable to clinical site for androgen deprivation—13% and 14% for primary and neoadjuvant therapy, respectively—are slightly lower than those observed in the SEER-Medicare analysis,<sup>9</sup> perhaps reflecting better control for patient and tumor factors in CaPSURE. What is striking, however, is the fact that site-specific variation was higher for every other treatment modality than for androgen ablation therapy (Table 2). Use of prostatectomy varied from 11% to 82%, nearly as great a range as the 10-fold variation observed in the Dartmouth Atlas of Health Care project.<sup>8</sup>

Explanations for the observed variation are speculative, but presumably reflect variable physician training, experience, and personal outcomes; payor mix, reimbursement patterns, and other financial incentives; the local medicolegal environment; uneven penetrance of novel technologies; impact of local culture on patient beliefs and preferences; and many other factors. An aggressive local or personal philosophy with respect to prostate cancer screening may also correspond to an increased tendency toward treatment, even controlling for varying stage at presentation. A similar observation has been made, for example, in correlating rates of coronary angiography with angioplasty and/or bypass surgery.<sup>8</sup> The protracted time course of prostate cancer, the proliferation of treatment options, and the nature of the potential complications of treatment all likely contribute additionally to the problem in the case of prostate cancer.

Certainly the absence of high-quality comparative effectiveness data, along with controversy regarding interpretation of the data that do exist, creates a fertile substrate in which variation would be ex-

pected to thrive. Even where high-quality evidence exists, however, incorporation into clinical practice may be variable. Randomized trials supporting the use of androgen deprivation together with radiation therapy, for example, were reported in the late 1990s, and those finding no benefit for androgen deprivation given before prostatectomy were reported in the early 2000s.<sup>21</sup> Within a few years, the use of androgen deprivation therapy with external-beam radiation for high-risk patients rose to 85%, whereas use of such therapy before prostatectomy appeared to be rising to more than 10% by the mid-to late-2000s.<sup>16,21</sup>

Caveats to this analysis must be noted, the most important of which is that although the practices in CaPSURE represent a range of practice sizes and geographic locations, they were not chosen at random and do not represent a statistically valid sample of the US population. We have previously compared the CaPSURE population to the SEER population of prostate cancer patients and found that the median age among patients is similar, though white men are relatively over-represented in CaPSURE compared with the general population.<sup>13</sup> Previous studies have found that race and ethnicity have little impact on degrees of variation in health care.<sup>22</sup> Men in CaPSURE also have slightly higher socioeconomic status on average than the overall population.<sup>11</sup> It is reassuring that the findings with respect to variation in use of prostatectomy and androgen deprivation therapy are generally consistent with the previous analyses from Medicare and SEER-Medicare; certainly there is no reason to suspect that the current analysis underestimates the true extent of variation at the population level.

Data in CaPSURE are submitted only by patients and urologists; thus any treatments by other clinicians that are not reported by patients either to their urologists or in their resource utilization questionnaires may be missed. Extant quality assurance mechanisms, including medical records review of all hospital admissions, is expected to minimize this problem. Despite these cautionary notes, we believe our data provide the best available description of case-mix adjusted national practice patterns.

Examination of treatment patterns in a large, national disease registry confirms substantial practice-level variation in management of localized prostate cancer that cannot be explained by disease case-mix variability. A growing body of evidence suggests that improved decision support may not only improve decision quality<sup>23</sup> and reduce decisional regret<sup>24</sup> but may also be a means to reduce unwarranted variation in health care.<sup>7</sup> Incorporation of such decision support into clinical practice, while challenging, should be a priority. Even more important is the need for better data on outcomes of prostate cancer treatment. The Institute of Medicine recently included treatment for localized prostate cancer among the 25 most important topics for future comparative effectiveness research.<sup>25</sup> Only through such research, based on both prospective clinical trials and retrospective review of high-quality, clinically rich data sources, will clinicians and patient be able to assess more accurately the relative merits, risks, and costs of treatment alternatives and, by extension, to reduce variation in their selections among these alternatives.

#### AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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