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Patterns of Practice in the United States: Insights from CaPSURE on Prostate Cancer Management

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The Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) is a national disease registry of more than 10,000 patients with prostate cancer treated at 31 primarily community-based sites across the country. The database tracks oncologic and health-related quality-of-life outcomes. Because the urologists participating in the project treat according to their usual practices, CaPSURE facilitates the study of trends in disease-management strategies, offering a reflection of "real world" practice patterns. This review highlights key studies during the past several years that document downward risk migration, validates widely used prognostic nomograms, establishes prostate-specific antigen doubling time as a surrogate endpoint for disease-specific mortality, assesses the impact of treatment on patient-reported quality of life, and presents national trends in imaging test use and primary treatment strategies for localized disease.

Introduction

The management of prostate cancer has become increasingly complex throughout the past decade, with a proliferation of treatment alternatives available to clinicians and the situation complicated further by reports of various treatments used in a wide range of combinations. Earlier diagnosis and therapeutic advances have facilitated the increased use of aggressive local treatment. Although evidence increasingly supports a reduction in prostate cancer mortality with aggressive treatment of localized disease [1], the protracted natural history of the disease necessitates long periods of follow-up to reach clinically meaningful endpoints. Therefore, extended, costly studies often are required to adequately evaluate any given management strategy.

Management practices for prostate cancer are changing constantly and are subject to a myriad of clinical, scientific, demographic, and economic dynamics. Furthermore, practices may vary between academic and community settings and among individual institutions. In an effort to document trends at a national level in disease management and in oncologic and health-related quality of life (HRQOL) outcomes, the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) was founded in 1995 as a disease registry of men with all of the stages of prostate cancer. This review highlights some of the key studies deriving from the database, with a particular focus on insights into contemporary prostate cancer management.

The Cancer of the Prostate Strategic Urologic Research Endeavor

Structure and organization of the CaPSURE disease registry

CaPSURE is a longitudinal, observational database, inaugurated in 1995, of men with biopsy-proven prostate adenocarcinoma. CaPSURE enrolls patients from a core group of 31 urologic practice sites. Patients from an additional nine sites, which are no longer accruing patients, are still followed; a total of 40 sites are represented in the database. Four and three sites are based in university-associated and Veterans Affairs (VA) medical centers, respectively, accounting for 4.8% and 3.2% of the patients. At each practice site, all of the men with biopsy-proven prostate cancer are invited consecutively to join CaPSURE regardless of their disease stage or treatment history. Informed consent for participation is obtained from each patient under local institutional review board supervision.

CaPSURE collects approximately 1000 urologist- and patient-reported variables. Clinical information, collected from urologists at baseline and each time the patient returns for care, includes history of prostate cancer diagnosis, biopsies, pathology, staging tests, primary and subsequent treatments (radical prostatectomy [RP], external-beam radiotherapy [EBRT], brachytherapy, primary and neoadjuvant androgen deprivation therapy [PADT and NADT], cryosurgery, and watchful waiting [WW]), Karnof-

sky performance status scores, and medications. At each clinic visit, the urologist documents current disease status, new diagnoses, disease signs and symptoms, and changes in medications. Imaging studies, prostate-specific antigen (PSA) levels, and other laboratory test results are tracked closely. Between 1995 and 1997, 4459 men were recruited; the initial data were entered retrospectively for most of them. For patients accessioned since 1999, all data collection has been prospective.

At enrollment, each patient completes a questionnaire addressing sociodemographic variables, comorbidities, and baseline HRQOL. Every 6 months thereafter, patients are mailed a follow-up questionnaire. The HRQOL components of the questionnaires include extensively validated survey instruments addressing general and disease-specific HRQOL, satisfaction with care, and fear of recurrence. Other sections of the patient questionnaires comprehensively assess the use of health services in the past 6 months. All of the patient-reported hospitalizations and emergency department use are verified with patient permission by review of discharge summaries; length of stay, discharge status, discharge diagnosis, and procedures performed are recorded. Response rates to the questionnaires are approximately 75% at each mailing. Patients are followed until time of death or withdrawal from the study.

Additional details of the project methodology, including quality-assurance protocols, have been reported previously [2]. More information, including an up-to-date list of publications and abstracts derived from the database, is available on the Internet at www.capsure.net. CaPSURE is managed by the Urology Outcomes Research Group of the Department of Urology at the University of California, San Francisco and has been generously funded since its inception by a grant from TAP Pharmaceutical Products, Inc. (Lake Forest, IL).

The CaPSURE Patient Cohort

As of July 2003, there were 10,081 patients enrolled in CaPSURE. The median patient age at diagnosis is 67 years and nearly 75% of the men are between the ages of 60 and 79 years. Most of the patients are white, with roughly 10% black representation and 3.5% Latino, Asian, and other ethnicities. There is fairly even distribution across socioeconomic strata, which is assessed by education and income level. More than 50% of CaPSURE patients are insured by Medicare, with or without supplemental policies, and the remainder have a variety of health coverage types.

A study of 241 CaPSURE patients enrolled at VA medical centers found that they are much more likely than the general patient population to be black, to have lower income, less education, and more comorbidity at presentation. They also have significantly higher-risk disease with regard to PSA at diagnosis and biopsy Gleason score. They are more likely to undergo WW or receive PADT and are less likely to undergo definitive local therapy. These differences may impact on the external validity of VA-based prostate cancer studies with respect to external applicability to other patients, but the findings should be validated in larger cohorts of VA and non-VA patients [3].

The median PSA at diagnosis is 7.3 ng/mL. More than two thirds of patients with a known PSA at diagnosis present with a PSA of 10 ng/mL or less and nearly 50% of the patients were diagnosed with a PSA between 4 and 10 ng/mL. Most patients present with a biopsy Gleason score of 5 or 6 and with clinical stage T1 or T2 disease. Overall, patients are distributed roughly evenly among low-, intermediate-, and high-risk groups, as defined by D'Amico *et al*. [4]; however, over time, the proportion with low-risk disease has been increasing and that of high-risk disease has been decreasing [5]. RP is the most common primary treatment, followed sequentially by PADT, EBRT, brachytherapy, WW, and cryotherapy. Of those with known comorbidity data, 50% have zero or one comorbid illness.

Prostate Cancer Outcomes

Prostate cancer management trends, like those for any other disease process, are driven primarily by studies of outcomes conducted in academic centers. These are of course the natural setting for the development and initial testing of novel diagnostic and therapeutic interventions; however, efficacy in academic studies does not translate uniformly to effectiveness in community practice because of far greater variability in patient characteristics and in the details of clinical intervention in the community than in the controlled setting of even the largest multicenter trials. As a community-based disease registry, CaPSURE has proved to be an excellent source of data for prostate cancer studies reflecting "real world" trends. It has provided an ideal means of validating hypotheses generated from smaller databases. Moreover, particularly as the number of evaluable patients has grown, CaPSURE has enabled studies requiring very large sample sizes to achieve sufficient statistical power.

Risk migration: temporal trends in clinical risk characteristics at presentation

Temporal trends during the PSA era in patient risk characteristics at diagnosis have been analyzed. The proportion of patients presenting with low-risk disease (*ie*, PSA ≤ 10 ng/mL, Gleason score under 7 with no pattern 4 or 5 disease on biopsy, and clinical stage T1 or T2a) [4] has increased from 31% of patients between 1989 and 1990 to 47% between 2001 and 2002. Conversely, high-risk diagnoses (PSA > 20 ng/mL, Gleason 8–10 biopsy, or stage T3-T4) [4] have decreased from 41% to 15% of patients. During the same time, those with high-risk disease T1 tumors became increasingly prevalent, as did those with Gleason 7 biopsies and those associated with a PSA of 4 to 10 ng/mL. In the early years of the study, patients were most likely to be classified as high-risk

because of a high PSA level; however, more recently, they were more likely to have a low PSA and a high Gleason score [5]. Smith *et al.* [6] previously have shown that Gleason scores have been increasing throughout the past decade as a result of changes in pathologic grading practices. Because this latter trend likely is artifactual rather than reflective of changes in cancer biology, it may be that as patients are being diagnosed with high-risk disease less commonly, a contemporary patient considered to be at high-risk could have a better prognosis as a result of more favorable tumor biology than an earlier high-risk patient.

A growing body of literature suggests that information derived from the results of the diagnostic biopsy contributes significantly to accurate risk assessment among patients with newly diagnosed localized disease [7–9]. The percent of positive biopsy cores was validated as a prognostic marker in newly diagnosed prostate cancer among 1265 RP patients in CaPSURE, 320 (25%) of whom experienced a recurrence at a median of 3.3 years. PSA at diagnosis, biopsy Gleason score, percent of positive biopsies, and black ethnicity were significant independent predictors of disease recurrence. The percent of biopsies that were positive was a significant predictor of disease recurrence within each of the low-, intermediate-, and high-risk groups, confirming that it may be a useful variable to identify patients with adverse risk features who may be appropriate for aggressive local therapy or those who may benefit from adjuvant treatment. Also significant is the confirmation that biopsy data obtained in the community, using nonstandardized techniques and assessed by diverse pathologists, offer consistently useful prognostic information [10].

Outcome prediction: nomogram validation studies

External validation is a crucial step in the development of nomograms and other risk prediction tools; the availability of CaPSURE and other large community-based cohorts provides an excellent means of assessing the external applicability of instruments developed in university-based patient series. Partin *et al.* [11] developed tables designed to predict pathologic outcomes after RP using the preoperative PSA, Gleason score, and clinical stage. These tables were developed and validated among patients from three academic institutions and are widely used in academic and community settings. Their performance in the community setting was assessed among 1162 CaPSURE patients who were undergoing RP. The receiver operating curve values were 0.684 for predicting organ-confined disease, 0.614 for capsular penetration, 0.726 for seminal vesicle involvement, and 0.766 for lymph node involvement. Although these values indicate good performance, particularly for predicting seminal vesicle and lymph node involvement, they are lower than those reported in the original academic series, perhaps because of differences in case mix in terms of baseline risk in the community setting [12].

The Partin tables predict pathologic rather than clinical outcomes. Therefore, CaPSURE data also have been used to validate risk assessment instruments based on the probability of biochemical recurrence or second treatment. For example, one nomogram developed by Bauer *et al.* [13] stratifies patients to low (72% recurrence-free survival [RFS]), intermediate (42% RFS), or high (28% RFS) risk of recurrence based on preoperative PSA, pathologic stage, postoperative Gleason sum, and ethnicity. This model was validated and refined using data combined from CaPSURE and the Department of Defense Center for Prostatic Disease Research (CPDR) database. Because the validation study included a much larger cohort (1515 patients, 1012 from CaPSURE, and 503 from CPDR), stratification could be improved using the same variables to four levels with very low (85% RFS), low (66% RFS), high (51% RFS), and very high (21% RFS) risk of recurrence [14].

A similar validation study, using CaPSURE patients only, has been undertaken for the nomogram developed by Kattan *et al.* [15], which predicts 5-year RFS based solely on the preoperative parameters: PSA at diagnosis, Gleason score, and clinical T stage. Similar to the Partin tables, the Kattan nomogram was developed in an academic setting and has subsequently been validated in a cohort drawn from multiple academic institutions [16]. Among 1701 RP patients in CaPSURE, 24% of whom experienced biochemical recurrence or were administered a second treatment, the overall concordance index for nomogram-predicted survival vis-à-vis actual RFS was 0.68, which is somewhat lower than that calculated from the academic validation cohort. In particular, the Kattan nomogram tends to overestimate survival among community patients at relatively low risk for recurrence [17]. The authors are working to develop a novel prognostic index with better applicability in the community setting and with improved simplicity of use.

CaPSURE data have been used further in conjunction with single-institution data from the University of California, San Francisco to examine prognostic factors among high-risk patients undergoing surgery. Among patients with a PSA higher than 20 ng/mL, a Gleason score ≥ 8, or stage T2c or higher, PSA, Gleason score, and the percent of positive biopsies independently predicted recurrence at 3 years; stage and age did not. The study also demonstrated a synergistic effect of Gleason and PSA in determining the risk of recurrence; among patients with a PSA higher than 20 ng/mL at diagnosis, those with a Gleason score lower than 8 had 45% RFS at 5 years compared with 0% of those with a score between 8 and 10. Conversely, among those with Gleason 8 to 10 biopsies, patients with a PSA lower than 10 ng/mL had 47% RFS compared with 19% for those with a PSA higher than 10 ng/mL [18].

CaPSURE data have allowed an analysis of the impact of ethnicity on biochemical recurrence after RP. Ethnicity was a strong predictor of risk-stratified outcomes in general. The greatest difference in outcomes was between

black and white patients with high-risk characteristics; 5-year biochemical RFS rates were estimated to be 65% among white patients and 28% among black patients. However, in a multivariate analysis controlling for income and education, variables that are associated closely with ethnicity, ethnicity was not an independent predictor of outcome [19].

Prostate-specific antigen doubling time

The protracted natural history of prostate cancer complicates the planning of clinical research trials because years of follow-up may be required to reach even surrogate endpoints such as biochemical recurrence and years more to identify the impact of treatments on firmer endpoints such as disease-specific mortality. Biochemical recurrence typically is defined by a PSA increase above a low threshold, typically 0.2 ng/mL, for RP patients and by three consecutive increases above a nadir for radiation therapy patients. Although widely reported, these biochemical surrogate endpoints do not reliably predict ultimate cause-specific mortality and, because the definitions are not consistent, they do not allow comparisons among differing treatment modalities such as RP and radiation therapy.

D'Amico *et al.* [20•] combined data from the CaPSURE and CPDR registries to conduct an analysis of post-treatment PSA kinetics among 8669 patients (5918 RP patients and 2751 radiation therapy patients). They identified post-recurrence PSA doubling time (PSADT) of less than 3 months as a powerful predictor of cause-specific mortality (hazard ratio = 19.6, $P < 0.001$) and overall mortality (hazard ratio = 6.9, $P < 0.001$) for RP and radiation patients. Primary treatment did not significantly predict cause-specific ($P = 0.37$) or overall ($P = 0.74$) mortality. For patients with a PSADT of more than 3 months, there was a continuous, inverse association between PSADT and time to cause-specific and overall mortality, regardless of treatment. PSADT as analyzed in this study is the first PSA-based surrogate endpoint to meet Prentice's criteria: that the surrogate marker predict disease-specific mortality and that the time to disease-specific mortality given the surrogate marker (*ie,* PSADT < 3 months) be independent of treatment received [20•]. These findings, possible only with the numbers of patients and extended follow-up present in large disease registries, suggest that PSADT may function as a valid short-term endpoint for future studies of prostate cancer therapeutics.

The effects of treatment on health-related quality of life

The extended natural history of localized prostate cancer mandates a high standard for HRQOL outcomes because patients may not feel any side effects of treatment for decades. All of the available treatments can affect patient HRQOL [21]; because of the excellent long-term survival after treatment for low-risk tumors, recent literature on localized disease has focused more on minimizing the morbidity of therapy than on oncologic outcomes. CaPSURE quality-of-life data have proven to be invaluable resources for the prospective, longitudinal assessment of patient-reported HRQOL outcomes and have successfully addressed a number of questions in this area of prostate cancer research.

An early CaPSURE HRQOL study highlighted the importance of studying patient-reported HRQOL data, finding that physician assessment of the HRQOL impact of treatment consistently underestimates the impact experienced by patients, particularly in general health domains [22]. Another study addressing sexual function after prostate cancer treatment divided men into "potent" or "impotent" groups based on objective criteria and analyzed scores on the sexual function and bother domains of the patient-reported Prostate Cancer Index between the two groups. Although there were significant differences between the mean scores of two groups, there also was broad overlap in scores, highlighting the importance of multidimensional patient-reported HRQOL assessment [23].

Litwin *et al.* [24] examined urinary function and bother among patients undergoing RP or EBRT. Immediately after treatment, urinary function (which assesses incontinence rather than irritative symptoms) was significantly worse among RP than EBRT patients. However, by 1 year after surgery, the urinary function of RP patients approached that of EBRT patients and remained stable during the second year. In contrast, urinary bother after treatment was worse among EBRT patients than among RP patients throughout the 2-year study period [24].

Another study by Litwin *et al.* [25] compared sexual function and bother between men undergoing RP and EBRT. Similar to the urinary function study, sexual function was better in the EBRT group immediately after treatment and the RP and EBRT groups showed improvement during the first year. During the second year, the RP patients continued to improve, but the EBRT patients started to show a significant decline. This decline after EBRT was greatest among older patients; after RP, older patients approached their low baseline level of function by 2 years. Sexual function was significantly better among RP patients who received nerve-sparing and among those using erectile aids [25]. The results from the urinary and sexual function studies concur with and validate those previously reported in a single-center cohort [26].

Prostate Cancer Management: National Practice Patterns

A great strength of the CaPSURE registry, which has made it an ideal source of data for the study of national practice patterns, is that all of the participating urologists, most of whom are community-based, treat patients according to their usual practice preferences, not following any specified protocols or guidelines. The patients, overwhelmingly diagnosed during the PSA era, remain eligible for other

clinical trials and any treatments associated with such trials are reported as they are received. Thus, the database offers as good of a reflection of contemporary urology practice at the national level as is available.

Imaging tests for disease staging

One of the first studies published from CaPSURE data was an analysis of imaging test use for staging clinically localized prostate cancer. Kindrick *et al.* [27] analyzed rates of bone scan, computed tomography, and magnetic resonance imaging testing between 1989 and 1997 and compared actual practice patterns to recommendations in the literature. They found broad and consistent overuse with regard to testing among patients with low PSA and Gleason scores, among whom the likelihood of extraprostatic disease is low. Furthermore, there was little change in testing rates over the study period, even as the median PSA fell 25% during the course of the study [27].

However, a follow-up study reporting data through 2001 found that rates of bone scan and cross-sectional imaging have fallen dramatically since the first analysis. Whereas during the first years of the study, disease risk (assessed by PSA, Gleason score, and clinical T stage) had minimal bearing on the likelihood of testing (80%, 82%, and 82% of low-, intermediate-, and high-risk patients, respectively, imaged between 1989 and 1990, $P = 0.81$), the likelihood of testing has become highly associated with risk group (20%, 49%, and 69% imaged between 2000 and 2001, respectively; $P < 0.0001$) in more recent years [28]. There was nearly a 10-fold variation in the rates of use among individual CaPSURE sites. Pre-treatment imaging tests serve to facilitate optimal treatment planning by increasing the accuracy of clinical staging. However, such investigations are associated with low but definite risks and with significant costs to the health care system. CaPSURE data have illustrated a strong trend toward a more appropriate use of imaging tests, increasingly evidence-based and driven by the clinical risk characteristics, which estimate the prior probability of the staging tests.

Trends in primary treatment selection

A number of recent CaPSURE studies have examined patterns in primary treatment selection for patients with localized prostate cancer. The first was an analysis of temporal trends in the use of androgen ablation therapy for localized prostate cancer. Cooperberg *et al.* [29•] examined the use of PADT and NADT among patients with localized disease of various risk levels. The use of PADT as monotherapy has increased dramatically across groups over the past decade (from 5% to 14%, 9% to 20%, and 33% to 48% among low-, intermediate-, and high-risk patients, respectively, from 1989–1990 to 2000–2001). Likewise, the use of NADT has increased from 3% to 8% of patients undergoing RP, 10% to 75% of those receiving EBRT, and 7% to 25% of those receiving brachytherapy. Older patients and those of lower socioeconomic status were more likely to receive PADT and NADT [29•].

The breadth of the observed increases in hormonal therapy appear to extend beyond those supported by recent literature. The American Urological Association's clinical practice guidelines consider PADT monotherapy to be investigational [30] and no controlled trials have established the efficacy of this approach. Good evidence supports the use of NADT in association with radiotherapy in high-risk disease [31,32]. In contrast, other recent studies of patients with more favorable risk factors have demonstrated that NADT before prostatectomy does not improve outcomes [33]. Likewise, the benefit for NADT before radiotherapy appears to be restricted to patients with higher-risk tumors. In the case of brachytherapy, NADT results in effective cytoreduction, but does not change clinical outcomes [34].

The findings of increasing hormonal therapy use were somewhat surprising in the context of earlier disease detection and decreasing risk migration (we would have expected increasing use of active surveillance as a first approach, particularly among low-risk patients with low disease burden). Because of the prolonged natural history of localized prostate cancer and the HRQOL impact of all of the available active treatments, a growing body of research supports WW as a viable alternative for at least the initial management of carefully selected patients with favorable risk characteristics [35,36].

An early cross-sectional analysis from CaPSURE found that only 8.2% of patients in the database pursued WW as primary management; these were mostly older patients and those with favorable risk parameters [37]. More recently, Harlan *et al.* [38•] examined trends over time in WW use, finding that WW use has fallen from 9.5% in 1992–1994 to 5.5% in 1998–2000. As in the cross-sectional study, older patients, those at lower risk, and those with greater comorbidity were more likely to opt for WW [38•].

Treatment trends among low-risk patients during the PSA era have been studied with greater detail, finding that the use of WW among low-risk patients has fallen by more than 50%, from 20% of patients in 1993–1995 to 8% in 1999–2001. Over the same time, the use of EBRT fell from 13% to 7% while that of RP fell slightly, from 55% to 52%. In contrast, the use of PADT and brachytherapy increased significantly, from 7% to 12% and from 4% to 22%, respectively. Even among patients 75 years of age or older, WW use decreased from 52% to 24%, while PADT increased from 23% to 30% and brachytherapy from 3% to 31% of patients [39].

In the cross-sectional study, more than 50% of the WW patients underwent secondary treatment within 5 years, especially those who were younger or had higher PSA scores at the time of diagnosis [40]. Most of these received androgen deprivation therapy. Another recent study has identified predictors of eventual treatment among WW patients, finding that PSA kinetics were a strong driver of treatment decisions. Patients with a PSA increase of more

than 5 ng/mL were nearly four times as likely to opt for treatment as those with an increase less than 2 ng/mL. High-risk baseline characteristics also were significant predictors of eventual active treatment [38•].

The resource use data in CaPSURE offer a means of studying health care system-wide cost implications of various management strategies for prostate cancer. Penson *et al.* [41] analyzed the stage-adjusted first-year costs associated with various treatment options based on Medicare payment schedules. They found that the mean cost of prostate cancer treatment in the first year after diagnosis was $6375, with a trend toward significantly higher costs for higher-stage patients. Costs were not different between RP and EBRT patients, but were significantly higher for patients receiving NADT before either primary treatment [41].

The explanation for the trends observed (most notably, across-the-board increases in hormonal therapy use for localized disease and decreased use of active surveillance) is almost certainly multifactorial, encompassing a number of patient- and physician-driven clinical, psychologic, medicolegal, and economic factors. They raise the concern that many patients may be overtreated, particularly older patients receiving multimodal therapy for low-risk disease. The extent to which these trends respond to ongoing developments in the literature and to continuing evolution of health care delivery systems will continue to be an active avenue of research.

Conclusions

The interpretation of CaPSURE data is subject to several caveats. Data on many patients accessioned before 1998 were entered retrospectively and thus may be vulnerable to reporting bias. At least one prior analysis found no difference in resource use data between patients whose data were entered prospectively or retrospectively [27]. Although CaPSURE represents a mix of locales and practice types, the sites have not been chosen at random and thus cannot be assumed to represent a statistically valid sample of US practice patterns. For example, white patients are relatively overrepresented in CaPSURE compared with national census data. Only diagnostic and therapeutic interventions ordered or coordinated by participating urologists are recorded. Patient reports of resource use and review of hospital records, described previously, help to minimize this potential treatment bias. Despite these cautionary notes, the authors believe their data provide the best available description of national practice patterns. Patient enrollment continues and, as longer follow-up data are collected, CaPSURE will be an increasingly valuable source of data on oncologic and HRQOL outcomes, which is exactly what is needed to inform future developments in prostate cancer treatment. The database also will continue to be an invaluable source of epidemiologic data and a unique means of monitoring national trends in prostate cancer management.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1. Holmberg L, Bill-Axelson A, Helgesen F, *et al.*: **A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer.** *N Engl J Med* 2002, **347:**781–789.
2. Lubeck DP, Litwin MS, Henning JM, *et al.*: **The CaPSURE database: a methodology for clinical practice and research in prostate cancer. CaPSURE Research Panel. Cancer of the Prostate Strategic Urologic Research Endeavor.** *Urology* 1996, **48:**773–777.
3. Cooperberg MR, Lubeck DP, Penson DF, *et al.*: **Sociodemographic and clinical risk characteristics of patients with prostate cancer within the Veterans Affairs health care system: data from CaPSURE.** *J Urol* 2003, **170:**905–908.
4. D'Amico AV, Whittington R, Malkowicz SB, *et al.*: **Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer.** *JAMA* 1998, **280:**969–974.
5. Cooperberg MR, Lubeck DP, Mehta SS, Carroll PR: **Time trends in clinical risk stratification for prostate cancer: implications for outcomes (Data from CaPSURE).** *J Urol* 2003, **170:**S21–S27.
6. Smith EB, Frierson HF Jr, Mills SE, *et al.*: **Gleason scores of prostate biopsy and radical prostatectomy specimens over the past 10 years: Is there evidence for systematic upgrading?** *Cancer* 2002, **94:**2282–2287.
7. Presti JC Jr, Shinohara K, Bacchetti P, *et al.*: **Positive fraction of systematic biopsies predicts risk of relapse after radical prostatectomy.** *Urology* 1998, **52:**1079–1084.
8. D'Amico AV, Whittington R, Malkowicz SB, *et al.*: **Clinical utility of the percentage of positive prostate biopsies in defining biochemical outcome after radical prostatectomy for patients with clinically localized prostate cancer.** *J Clin Oncol* 2000, **18:**1164–1172.
9. Freedland SJ, Csathy GS, Dorey F, Aronson WJ: **Percent prostate needle biopsy tissue with cancer is more predictive of biochemical failure or adverse pathology after radical prostatectomy than prostate-specific antigen or Gleason score.** *J Urol* 2002, **167:**516–520.
10. Grossfeld GD, Latini DM, Lubeck DP, *et al.*: **Predicting disease recurrence in intermediate and high-risk patients undergoing radical prostatectomy using percent positive biopsies: results from CaPSURE.** *Urology* 2002, **59:**560–565.
11. Partin AW, Yoo J, Carter HB, *et al.*: **The use of prostate-specific antigen, clinical stage, and Gleason score to predict pathological stage in men with localized prostate cancer [see comments].** *J Urol* 1993, **150:**110–114.
12. Penson DF, Grossfeld GD, Li YP, *et al.*: **How well does the Partin nomogram predict pathological stage after radical prostatectomy in a community based population? Results of the cancer of the prostate strategic urological research endeavor.** *J Urol* 2002, **167:**1653–1658.
13. Bauer JJ, Connelly RR, Seterhenn IA, *et al.*: **Biostatistical modeling using traditional preoperative and pathological prognostic variables in the selection of men at high risk for disease recurrence after radical prostatectomy for prostate cancer.** *J Urol* 1998, **159:**929–933.
14. Moul JW, Connelly RR, Lubeck DP, *et al.*: **Predicting risk of prostate-specific antigen recurrence after radical prostatectomy with the Center for Prostate Disease Research and Cancer of the Prostate Strategic Urologic Research Endeavor databases.** *J Urol* 2001, **166:**1322–1327.

15. Kattan MW, Eastham JA, Stapleton AM, *et al.*: **A preoperative nomogram for disease recurrence following radical prostatectomy for prostate cancer.** *J Natl Cancer Inst* 1998, **90:**766–771.
16. Graefen M, Karakiewicz PI, Cagiannos I, *et al.*: **International validation of a preoperative nomogram for prostate cancer recurrence after radical prostatectomy.** *J Clin Oncol* 2002, **20:**3206–3212.
17. Cooperberg MR, Greene KL, Grossfeld GD, *et al.*: **Validation of the Kattan pre-treatment nomogram in community patients undergoing radical prostatectomy: results from CaPSURE [Abstract].** *J Urol* 2003, **169:**1661.
18. Grossfeld GD, Latini DM, Lubeck DP, *et al.*: **Predicting recurrence after radical prostatectomy for patients with high risk prostate cancer.** *J Urol* 2003, **169:**157–163.
19. Grossfeld GD, Latini DM, Downs T, *et al.*: **Is ethnicity an independent predictor of prostate cancer recurrence after radical prostatectomy?** *J Urol* 2002, **168:**2510–2515.
20.• D'Amico AV, Moul JW, Carroll PR, *et al.*: **Surrogate end point for prostate cancer-specific mortality after radical prostatectomy or radiation therapy.** *J Natl Cancer Inst* 2003, **95:**1376–1383.

If validated in future studies, PSADT may prove to be the first biochemical surrogate that actually predicts mortality outcomes across various treatment types.

21. Wei JT, Dunn RL, Sandler HM, *et al.*: **Comprehensive comparison of health-related quality of life after contemporary therapies for localized prostate cancer.** *J Clin Oncol* 2002, **20:**557–566.
22. Litwin MS, Lubeck DP, Henning JM, Carroll PR: **Differences in urologist and patient assessments of health related quality of life in men with prostate cancer: results of the CaPSURE database.** *J Urol* 1998, **159:**1988–1992.
23. Cooperberg MR, Koppie TM, Lubeck DP, *et al.*: **How potent is potent? Evaluation of sexual function and bother in men who report potency after treatment for prostate cancer: data from CaPSURE.** *Urology* 2003, **61:**190–196.
24. Litwin MS, Pasta DJ, Yu J, *et al.*: **Urinary function and bother after radical prostatectomy or radiation for prostate cancer: a longitudinal, multivariate quality of life analysis from the Cancer of the Prostate Strategic Urologic Research Endeavor.** *J Urol* 2000, **164:**1973–1977.
25. Litwin MS, Flanders SC, Pasta DJ, *et al.*: **Sexual function and bother after radical prostatectomy or radiation for prostate cancer: multivariate quality-of-life analysis from CaPSURE. Cancer of the Prostate Strategic Urologic Research Endeavor.** *Urology* 1999, **54:**503–508.
26. Talcott JA, Rieker P, Clark JA, *et al.*: **Patient-reported symptoms after primary therapy for early prostate cancer: results of a prospective cohort study.** *J Clin Oncol* 1998, **16:**275–283.
27. Kindrick AV, Grossfeld GD, Stier DM, *et al.*: **Use of imaging tests for staging newly diagnosed prostate cancer: trends from the CaPSURE database.** *J Urol* 1998, **160:**2102–2106.
28. Cooperberg MR, Lubeck DP, Grossfeld GD, *et al.*: **Contemporary trends in imaging test utilization for prostate cancer staging: data from the cancer of the prostate strategic urologic research endeavor.** *J Urol* 2002, **168:**491–495.
29.• Cooperberg MR, Grossfeld GD, Lubeck DP, Carroll PR: **National practice patterns and time trends in androgen ablation for localized prostate cancer.** *J Natl Cancer Inst* 2003, **95:**981–989.

A detailed presentation of national trends in use of primary and neoadjuvant hormonal therapy for localized prostate cancer, in the context of current evidence for and against these treatment strategies.

30. American Urological Association Prostate Cancer Clinical Guidelines Panel: **Report on the management of clinically localized prostate cancer.** *J Urol* 1995, **154:**2144–2148.
31. Bolla M, Gonzalez D, Warde P, *et al.*: **Improved survival in patients with locally advanced prostate cancer treated with radiotherapy and goserelin.** *N Engl J Med* 1997, **337:**295–300.
32. Pilepich MV, Caplan R, Byhardt RW, *et al.*: **Phase III trial of androgen suppression using goserelin in unfavorable-prognosis carcinoma of the prostate treated with definitive radiotherapy: report of Radiation Therapy Oncology Group Protocol 85-31.** *J Clin Oncol* 1997, **15:**1013–1021.
33. Soloway MS, Pareek K, Sharifi R, *et al.*: **Neoadjuvant androgen ablation before radical prostatectomy in cT2bNxM0 prostate cancer: 5-year results.** *J Urol* 2002, **167:**112–116.
34. Potters L, Torre T, Ashley R, Leibel S: **Examining the role of neoadjuvant androgen deprivation in patients undergoing prostate brachytherapy.** *J Clin Oncol* 2000, **18:**1187–1192.
35. Carter HB, Walsh PC, Landis P, Epstein JI: **Expectant management of nonpalpable prostate cancer with curative intent: preliminary results.** *J Urol* 2002, **167:**1231–1234.
36. Choo R, DeBoer G, Klotz L, *et al.*: **PSA doubling time of prostate carcinoma managed with watchful observation alone.** *Int J Radiat Oncol Biol Phys* 2001, **50:**615–620.
37. Koppie TM, Grossfeld GD, Miller D, *et al.*: **Patterns of treatment of patients with prostate cancer initially managed with surveillance: results from the CaPSURE database.** *J Urol* 2000, **164:**81–88.
38.• Harlan SR, Cooperberg MR, Elkin EP, *et al.*: **Time trends and characteristics of men choosing watchful waiting for initial treatment of localized prostate cancer: results from CaPSURE.** *J Urol* 2003, **170:**1804–1807.

This paper documents decreasing use of watchful waiting during the PSA era across all risk groups.

39. Cooperberg MR, Mehta SS, Lubeck DP, *et al.*: **The changing face of low-risk prostate cancer: trends in clinical presentation and treatment patterns (data from CaPSURE) [Abstract].** *J Urol* 2003, **169:**1723.
40. Koppie TM, Grossfeld GD, Miller D, *et al.*: **Patterns of treatment of patients with prostate cancer initially managed with surveillance: results from The CaPSURE database. Cancer of the Prostate Strategic Urological Research Endeavor.** *J Urol* 2000, **164:**81–88.
41. Penson DF, Schonfeld WH, Flanders SC, *et al.*: **Relationship of first-year costs of treating localized prostate cancer to initial choice of therapy and stage at diagnosis: results from the CAPSURE database.** *Urology* 2001, **57:**499–503.