Title
Trends in Management for Patients With Localized Prostate Cancer, 1990-2013.

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Letters

RESEARCH LETTER

Trends in Management for Patients With Localized Prostate Cancer, 1990-2013

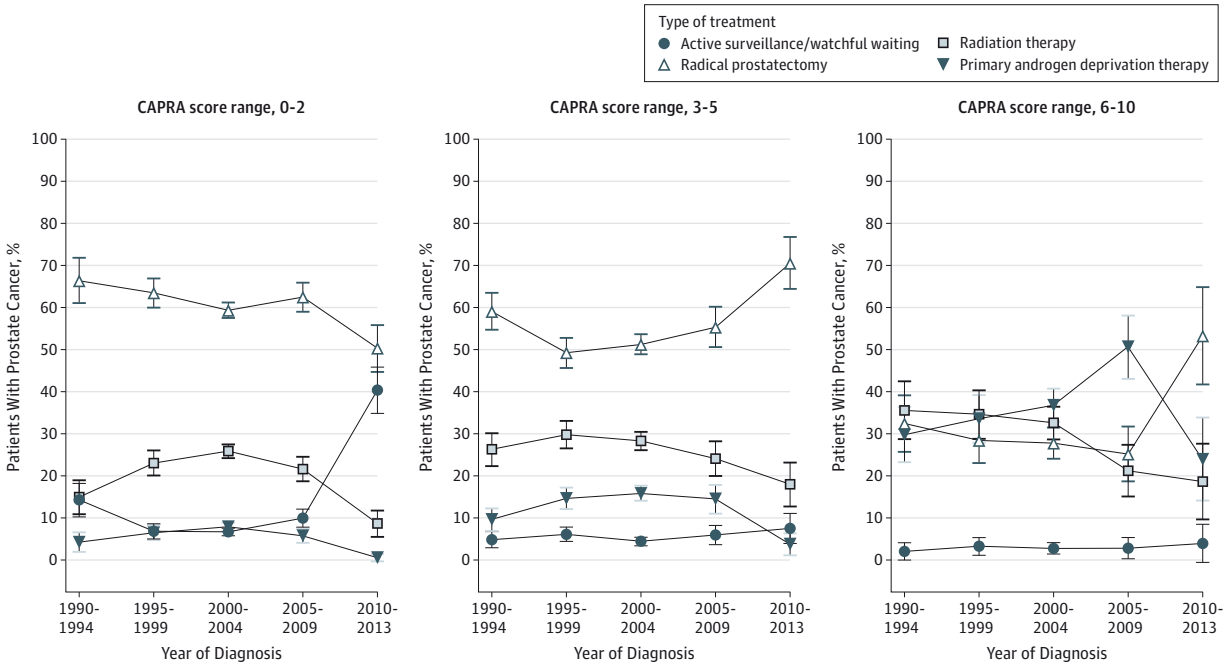
A growing literature supports the safety and efficacy of active surveillance for patients with low-risk prostate cancer. However, the experience behind this literature is based almost entirely in academic centers, and prior reports have consistently found surveillance generally underused in most other settings.[1,2] Conversely, high-risk tumors have been undertreated with androgen deprivation treatment alone.[2,3] Recent trends in community-based practice patterns have not been well documented.

Methods | Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) is a national registry accruing men with prostate cancer diagnosed at 45 urology practices across the United States since 1995. A mix of large and small practices are included. All but 3 are community-based practices and 28 states across all regions are represented. Both prospective enrollment of newly diagnosed men and retrospective enrollment of previously diagnosed men were permitted before 1998; however, since 1998 all enrollment has been prospective.

Approximately 90% of eligible patients are accrued. Urologists report clinical data; patients provide written consent under central institutional review board supervision. Other methodological details have been reported.[4] We analyzed men with tumors classified as stage cT3aN0M0 or lower managed with prostatectomy, radiation, androgen deprivation monotherapy, or active surveillance/watchful waiting between 1990 and 2013. Only recently have these 2 terms been clearly separated,[1] and CaPSURE has historically recorded them as a single category. There were 656 men (5.9%) with missing treatment data who were excluded.

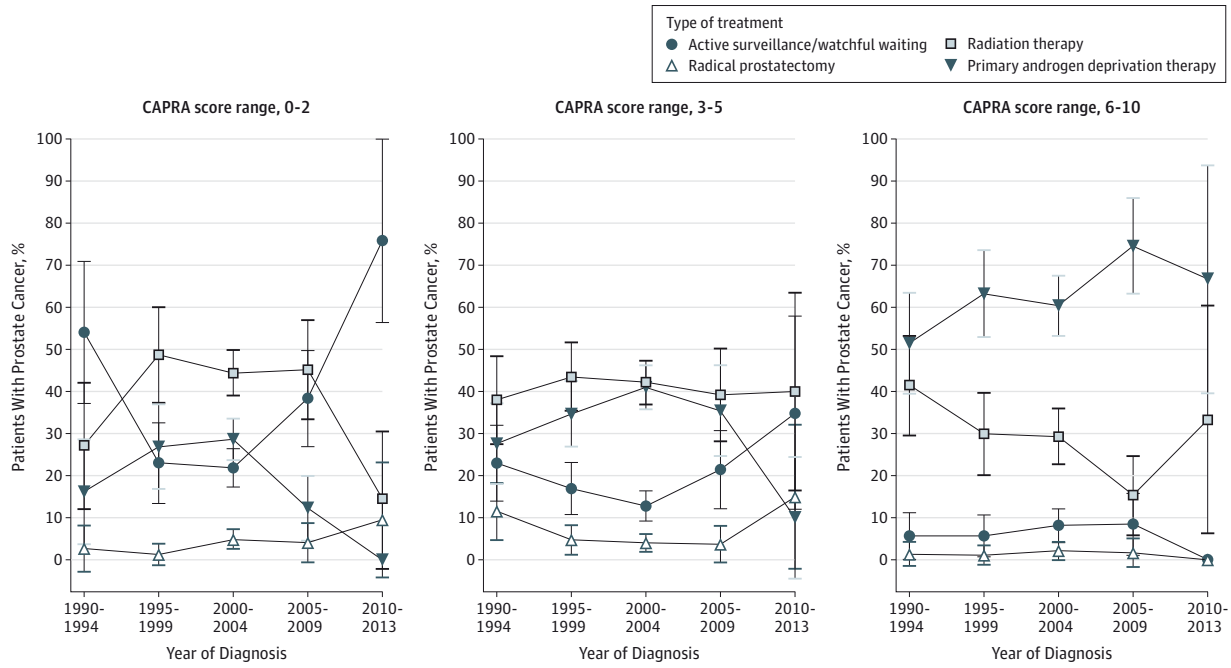
Cancer risk was stratified using the validated Cancer of the Prostate Risk Assessment (CAPRA) score.[5] We analyzed treatment trends over 5-year intervals in the full cohort and in a subset of men aged 75 years or older. We calculated Mantel-Haenszel tests for trends over time. There have been changes in the CaPSURE sites over time (eg, some have closed or withdrawn and others have been added). A subset analysis including only practices steadily contributing patients found substantially similar results. Analyses were performed with Stata version 12.1 (StataCorp). Statistical tests were 2-tailed with $\alpha = .05$.

Figure 1. Treatment Trends for the Overall Cohort in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) Registry



Error bars indicate 95% confidence intervals; CAPRA, Cancer of the Prostate Risk Assessment.

Figure 2. Treatment Trends for Older Men (≥75 Years of Age) in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) Registry



Error bars indicate 95% confidence intervals; CAPRA, Cancer of the Prostate Risk Assessment.

Results | Among 10 472 men included, the mean (SD) age was 65.7 (8.8) years. The median CAPRA score was 2 (interquartile range, 1-4). There were 1015 black men (9.7%) and 9111 white men (87.0%). Surveillance use for low-risk disease (CAPRA score range, 0-2) remained low from 1990 through 2009 (varying from 6.7% [95% CI, 5.8%-7.6%] to 14.3% [95% CI, 10.3%-18.3%]), but increased sharply in 2010 through 2013 (to 40.4% [95% CI, 34.9%-45.9%]; $P < .001$ for trend). Conversely, treatment with androgen deprivation for intermediate-risk and high-risk tumors, which had been increasing steadily from 1990 (9.7% [95% CI, 7.0%-12.3%] and 29.8% [95% CI, 23.3%-36.4%], respectively), decreased sharply (to 3.8% [95% CI, 1.2%-6.4%] and 24.0% [95% CI, 14.1%-33.9%], respectively) (**Figure 1**).

Among men aged 75 years or older, the rate of surveillance was 54.1% (95% CI, 37.2% to 70.9%) from 1990 through 1994, declined to 21.9% (95% CI, 17.4% to 26.4%) from 2000 through 2004, and increased to 76.2% (95% CI, 56.3% to 96.1%) from 2010 through 2013. There was an increase in the use of surgery for men aged 75 years or older with low-risk cancer to 9.5% (95% CI, −4.1% to 23.2%) and intermediate-risk cancer to 15.0% (95% CI, −2.1% to 32.1%); however, there was not an increase in use for those with high-risk cancer, among whom androgen deprivation still accounted for 66.7% (95% CI, 39.6% to 93.7%) of treatment (**Figure 2**).

Surveillance rates at individual urology practices ranged from 8.3% to 63.6% (median, 36.0%; interquartile range, 12.7%-54.1%).

Discussion | In this analysis of a longstanding, national registry, we found that after years of overtreatment for patients with low-risk prostate cancer, rates of active surveillance/watchful waiting for low-risk disease increased sharply in 2010 through 2013. Concurrently, high-risk disease was more often treated appropriately with potentially curative local treatment rather than androgen deprivation alone, although not in men aged 75 years or older. Substantial variation persisted in treatment patterns across individual practices, as observed previously.[2,6]

The major limitation of the study is that CaPSURE is not a random population sample. However, participating practices do reflect broadly varied characteristics,[2] and the patients have previously been shown to be similar to those included in the Surveillance, Epidemiology, and End Results registry in terms of demographics, though CaPSURE patients are more often white and have higher incomes.[5]

The magnitude and speed of the changes suggest a genuine change in the management of patients with prostate cancer in the United States, which could accelerate as more clinicians begin to participate in registry efforts. Given that overtreatment of low-risk disease is a major driver of arguments against prostate cancer screening efforts, these observations may help inform a renewed discussion regarding early detection policy in the United States.

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Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: Cooperberg.
Drafting of the manuscript: Cooperberg.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Cooperberg.
Obtained funding: All authors.
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COMMENT & RESPONSE

Discordant Interpretations of Breast Biopsy Specimens by Pathologists

To the Editor Dr Elmore and colleagues[1] reported levels of diagnostic concordance among pathologists in the interpretation of breast biopsy specimens. We believe that the study was flawed in its design, and the conclusions may create unnecessary quality concerns.

The study was not designed to evaluate the diagnostic systems currently in place to provide diagnoses by pathologists, but instead to evaluate individual pathologists under unrealistically restrictive conditions. In actual practice, interobserver consultation is commonplace, and an evolving norm is for pathology practices to mandate that certain types of abnormalities (including the types that were the subject of the study) be reviewed by multiple pathologists as part of formal quality assurance programs.[2]

The level of concordance between the study pathologists and the consensus diagnosis (75%) was no different than the degree of initial concordance reported for the 3 expert breast pathologists who developed the consensus diagnosis. There is no evidence that each individual on the expert panel performed any better in the study than the individual study pathologists as a group.

In addition, the interpretation of the study cases was limited to a single slide per case without the opportunity to pursue additional studies, and participants were required to choose a definitive diagnosis on every case, even those with borderline or equivocal features. This approach does not reflect actual pathology practice and clearly contributed to lowering the concordance rate. In actual practice, pathologists have access to, and frequently use, ancillary methods for diagnosis, ranging from simply acquiring additional histological sections from paraffin-embedded tissue blocks to acquiring more tissue from native samples to immunohistochemical analysis.

The mix of cases used in the study also paints an unrealistic picture as to the frequency of diagnostic gray zones encountered in practice. Difficult or problematic cases represent only a small minority of breast biopsies encountered in routine clinical practice. This study oversampled cases known to engender diagnostic variability. As a result, the level of concordance reported in the study is not representative of the degree of concordance seen among consecutive breast biopsies encountered in routine clinical practice.

We welcome future research that assesses the efficacy of current systems that are in place for the diagnosis of difficult breast lesions, rather than artificial studies that unrealistically isolate incomplete components of those systems.

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Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Finn reported being the president and Dr Holladay reported being the CEO of the American Society for Clinical Pathology.

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To the Editor I was one of the pathologists who participated in the study by Dr Elmore and colleagues.[1] Although the conclusions are appropriately measured based on the inherent constraints imposed by the design, I have significant misgivings about the validity of the study based on my personal experience.

My participation was contingent on the promise of receiving relevant feedback to improve my practice. The recruitment material stated the purpose of the study was to "identify ways in which we can improve breast cancer diagnosis." A single slide is certainly not the way I or most other pathologists practice. The investigators stated that there would be scheduled slides to review on a regular basis.

However, more often than not, slides were delayed, sometimes for weeks, sometimes indefinitely. The slides