Purpose of the Study. Prostate cancer is the most common non-skin malignancy and second most lethal tumor among men. With recent advances in prostate-specific antigen (PSA) testing and biopsies, prostate cancer is diagnosed at progressively earlier stages and with lower risk features. Most men diagnosed die with—rather than as a result of—prostate cancer. Despite this, patients are more likely now than a decade ago to undergo active treatment rather than surveillance. Men may be “over diagnosed” if diagnosis leads to active treatment and doesn’t improve their life span or quality of life.

This study presents contemporary prostate cancer data trends on disease presentation, natural history, and primary management. The report also considers new approaches to risk assessment that may facilitate improved and balanced decision-making at the time of diagnosis to guide low risk patients away from active treatments with their potential negative impacts on health-related quality of life (HRQOL—how a person’s health affects their ability to carry out normal social and physical activities) and to direct higher risk patients toward an appropriate aggressive therapy or therapies. Widely accepted primary therapies for prostate cancer include radical prostatectomy (RP), hormone (androgen suppression therapy – AST) external beam radiation or brachytherapy - radioactive “seeds” placed in direct contact with the prostate.

Study Population. The research used data from two large, nationally based, long-term observational databases, the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE™) and the Department of Defense Center for Prostate Disease Research (CPDR). Each comprise well over 10,000 patients and represent highly useful complementary sources of data. CaPSURE™, initiated in 1995, is primarily community-based and includes 31 urologic practice sites. Participating urologists report clinical data, and patients regularly self-report on treatments and HRQOL issues. The patients are treated according to their physicians’ usual practices. CPDR, the largest prostate cancer database in the nation, has collected data on men in the military with prostate cancer at Walter Reed Army Medical Center since 1994 and at eight other military sites around the country since 1997. CPDR includes full participation by radiation & medical oncologists and is used to standardize prostate cancer practice across military sites. Also, observational data is reported from two recent, long-established, observational Scandinavian studies that enrolled patients with relatively high stage disease & also from 20 years of data from the Connecticut Tumor Registry.

Results and Conclusions. The management of localized prostate cancer is in rapid evolution, but current trends in primary treatment do not necessarily reflect evolving screening and diagnosis methods that have resulted in the majority of prostate cancers being detected at earlier stages and lower risk levels. With wide availability of PSA screening and biopsies, and increasing accuracy in prediction of recurrence and progression, many patients diagnosed today are excellent candidates for either active surveillance or immediate local monotherapy. Despite the promise that surveillance holds for HRQOL preservation and potential treatment avoidance, its use has abruptly declined in recent years. (Active surveillance might be distinguished from watchful waiting on the basis of the intensity of monitoring and the expectation of delayed but successful definitive treatment for patients showing signs of disease progression.)

To avoid over treatment of indolent (slow to develop) prostate tumors that cause little or no pain or annoyance, treatment decisions must consider a patient’s life expectancy, quality of life at diagnosis and treatment preferences as well as the disease characteristics. Clinicians, therefore, must strive for a balance in offering treatment options to maximize HRQOL, odds of long-term disease control, and survival in a range of patients—such as conservative treatment for low risk patients of advanced age or in poor general health, to more aggressive treatment for younger patients with higher-risk cancer.
Natural History of Prostate Cancer. Recent research has looked at the natural progression of prostate cancer and the impact of local therapy on survival. One Scandinavian observational study confirmed that many tumors follow an indolent course for the first 10 to 15 years after diagnosis, but that prostate cancer-specific mortality (PCSM) triples beyond 15 years. A second Scandinavian study (the only randomized trial reported to date of initial surveillance vs. RP) found that after 5 years of follow-up, overall survival differed between initial surveillance and active treatment. Patients diagnosed younger than 65 years had a 19% risk of PCSM on surveillance, a rate cut nearly in half by surgery. Patients diagnosed older than 65 years had no statistically significant difference in mortality outcomes.

Although the two studies support a role for early treatment, they also strongly reinforce the importance of patient selection for aggressive therapy – as patients with low-risk tumors and/or without extended life expectancy may not benefit from early active treatment. Both studies enrolled prior to current advanced screening techniques and analyzed mostly patients at high risk for recurrence. Other recent studies indicate a significant number of diagnosed men (particularly older patients with low-risk disease) would not suffer any adverse impact to their quantity or quality of life were the cancer never detected.

Trends in Primary Management of Prostate Cancer. Data from the Prostate Cancer Outcomes Study (PCOS) collected from 1994 to 1995 found that only 19% of diagnosed patients chose surveillance. CaPSURE™ and CPDR data from the 1990s showed that it is older patients and those with low risk characteristics who are more likely to elect surveillance versus active treatment. A more recent analysis from CaPSURE™ showed that use of initial surveillance fell 4% from 1992 to 2000, with the sharpest declines among low-risk patients. Other recent CaPSURE™ data that focused on treatment of low-risk patients showed rates of surveillance fell 12% from 1993 to 2001. Even among patients 75 years of age or older, surveillance fell more than 20%.

Conversely, various studies show rising rates and a high use of primary androgen suppression therapy (AST) among localized prostate cancer patients. PCOS data suggests higher-than expected use; another study shows AST has risen dramatically across all patient groups during the last decade (1989-2001). Likewise, supplemental AST rose to 5% in patients undergoing prostatectomy, to 65% in those receiving external beam radiotherapy, and 18% in those receiving brachytherapy. Of high-risk patients in CaPSURE™, 52% of those managed primarily with radiation therapy received supplemental AST. Androgen suppression therapy is now well established to improve outcomes among men with high risk tumors who undergo radiation therapy.

Future Directions. Ongoing research continues to improve standard care in screening, diagnosis, risk assessment and primary management of prostate cancer. For example, obesity with its complex set of genetic, metabolic, dietary, environmental & non-medical social influences on health is being explored as potential risk factor for prostate cancer.

In addition, there are efforts to develop a better PSA test, which are driven by yet unresolved deficiencies in the accuracy of PSA screening to detect significant tumor. Also, additional research with large databases of prostate cancer patients has yielded new uses of information currently available in clinical practice, such as using the percentage of biopsy cores positive to increase the exactness of the prostate cancer prognosis, the development of the University of California San Francisco Cancer of the Prostate Risk Assessment (CAPRA; San Francisco, CA), a novel index that is notably easier than other methods to calculate and predict risk of recurrence after prostatectomy, and renewed attention on PSA kinetics (PSA velocity and PSA doubling time) for prognostic ability both before and after treatment. With improvements in screening techniques, it may be possible to more accurately detect high risk cancers and designate candidates for aggressive therapies, and allow more men to elect surveillance which can preserve their quality of life.

Article Citation: Cooperberg MR, Moul J, Carroll PR. The changing face of prostate cancer. Journal of Clinical Oncology. 2005;10; 8146-51.