Editorial Comment on: Development of a New Method for Monitoring Prostate-Specific Antigen Changes in Men with Localized Prostate Cancer: A Comparison of Observational Cohorts

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Prostate-specific antigen (PSA) kinetics remains a critical tool in prostate cancer (PCa) screening, diagnosis, and treatment, despite limitations. PSA, especially its changing rate (eg, PSA velocity [PSAV]), is associated with the status of PCa. Three randomized trials[em]the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial [1], the Prostate Cancer Prevention Trial (PCPT), and the European Randomized Study of Screening for Prostate Cancer (ERSPC) [2][em]have shown (1) that there is not a PSA cut-off value that can be determinative for prostate biopsy; (2) that lead time and overdiagnosis are the two quantifiers for the potential benefits and harms of PSA screening; and (3) that, different from clinically detected diseases, many of the screening-detected diseases are low risk and may be candidates for active surveillance. Carter et al reported PSAV of 0.75 ng/ml per year as a cut-off for prostate biopsy [3]. Our study shows that while PSAV of 0.75 ng/ml per year is good for cancer detection in men aged >70 yr, PSAV of 0.40 has the same sensitivity and specificity for men aged 50[en]60 yr [4[en]6].

An ideal tool for optimal PCa screening would enable prediction of the presence of PCa and differentiation of the tumor aggressiveness into clinically significant and latent cancer to avoid overdiagnosis that inevitably will lead to overtreatment; however, such a tool is not yet available.

This study, reported by Tilling et al [7], is among the few novel efforts moving in the direction of such a new tool. Using a multi-institutional data set, this group developed models to predict PSA trends. The unique point is that the predicted PSA value is age and Gleason score adjusted, so that using baseline PSA each year of the increased age and each grade of the increased biopsy Gleason score, the patient's future PSA values can be predicted and virtual PSAV can be calculated. If the models are validated, they may be the tool that is needed to avoid overdiagnosis and to select candidates for active surveillance.

References

- [1] Grubb RL III, Pinsky PF, Greenlee RT, et al. Prostate cancer screening in the Prostate, Lung, Colorectal and Ovarian cancer screening trial: update on findings from the initial four rounds of screening in a randomized trial. BJU Int 2008;102:1524[en]30.
- [2] Schröder FH, Bangma CH, Roobol MJ. Is it necessary to detect all prostate cancers in men with serum PSA levels <3.0 ng/ml? A comparison of biopsy results of PCPT and outcome-related information from ERSPC. Eur Urol 2008;53:901[en]8.

- [3] Carter HB, Ferrucci L, Kettermann A, et al. Detection of life-threatening prostate cancer with prostate-specific antigen velocity during a window of curability. J

 Natl Cancer Inst 2006;98:1521[en]7.
- [4] Moul JW, Sun L, Hotaling JM, et al. Age-adjusted PSA and PSA velocity cutpoint in prostate cancer screening. J Urol 2007;177:499[en]503.
- [5] Taneja SS. Re: age-adjusted PSA and PSA velocity cutpoint in prostate cancer screening. Eur Urol 2007;52:607.
- [6] Ankerst DP, Thompson IM. Understanding mixed messages about prostate specific antigen: biases in the evaluation of cancer biomarkers. J Urol 2007;177:426[en]7.
- [7] Tilling K, Garmo H, Metcalfe C, et al. Development of a new model for prostatespecific antigen reference ranges for monitoring men with localized prostate cancer: a comparison of observational cohorts. Eur Urol. In press.