AB004. Rational and risk-stratified prostate cancer screening and treatment

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Abstract: Global prostate cancer epidemiology has evolved in recent years, reflecting complex shifts in life expectancy, diet and lifestyle, and screening practices. Experience in the US over the past 20 years has clearly demonstrated that implementation of early prostate cancer detection through ad hoc prostate specific antigen (PSA) testing mostly of older men will lead to substantial rates of overdiagnosis, and potentially to avoidable harms of overtreatment—yet is largely responsible for a >50% reduction in age-adjust prostate cancer mortality rates. The recommendation of the US Preventive Services Task Force in 2012 that no men should be screened for prostate cancer has driven down both diagnosis of low-risk disease (less overdiagnosis) and high-risk disease (more under-diagnosis), and rates of metastatic disease at diagnosis are now rising. Emerging research suggests strongly that neither a "screen all" nor "screen none" approach is optimal—but rather than a smarter screening paradigm can further affect mortality reductions while simultaneously minimizing overtreatment. The best evidence from randomized trials suggests that relative prostate cancer mortality can be reduced by ~30–50% through screening, and most contemporary guidelines recommend shared decision making for men in their 50s to 60s, though there is disagreement regarding optimal starting age, and none of the guidelines comments on how to screen. Excellent cohort studies suggest that early (age 45–55) baseline testing, with subsequent intervals driven by baseline findings, may be optimal. PSA should not be interpreted in a vacuum, but rather considered in light of age, family history, race, physical exam findings, and other parameters, and calculators are available to facilitate such a multivariable assessment. Moreover, a growing array of secondary tests are available to help men with mildly elevated PSAs make decisions about biopsy—these include blood tests (4K, phi), urine tests (e.g., PCA3, MiPS, SelectMDx), and imaging tests (multiparametric MRI), each with strengths and limitations. At time of diagnosis, prostate cancers should be risk stratified, ideally using a multivariable instrument rather than a risk grouping system. A growing consensus supports active surveillance as the preferred strategy for most men with low grade (Gleason grade group 1) disease, and even for carefully selected men with grade group 2 tumors. These decisions may be further tailored with MRI and/or tissue-based biomarkers assessing gene expression patterns. Tailored approaches to screening and management—with deintensification of surveillance strategies for men with low risk disease, and intensified, multimodal approaches for those with high-risk disease—should allow both further gains in prostate cancer mortality reduction and minimization of the impact of avoidable overdiagnosis and overtreatment.

Keywords: Prostate cancer; excellent cohort study; prostate specific antigen (PSA)

doi: 10.21037/tau.2018.AB004

Cite this abstract as: Cooperberg MR. Rational and risk-stratified prostate cancer screening and treatment. Transl Androl Urol 2018;7(Suppl 5):AB004. doi: 10.21037/tau.2018.AB004

