The US Preventative Services Task Force recently recommended against routine prostate-specific antigen (PSA) screening for prostate cancer. Interpreting the results from clinical trials, the Task Force concluded that PSA screening provides "at most modest benefit, with unacceptable costs in terms of overdiagnosis and overtreatment." As an alternative, experts recommend more personalized or smarter screening strategies that preserve benefit while reducing harm. Unfortunately, it is unlikely that these strategies will be evaluated in randomized clinical trials due to constraints in resources and logistics.
To address this concern, Drs. Joshua Roth, Roman Gulati, Ruth Etzioni, and colleagues, used simulation modeling to conduct comparisons of candidate screening approaches. Specifically, the investigators examined whether smarter PSA screening strategies have the potential to be effective and cost-effective relative to no screening. In addition, they evaluated the potential added value of projecting outcomes under selective treatment practices with increased use of conservative management (consisting of an annual office visit, annual PSA testing, and a biennial biopsy) among men with screen-detected, low-risk disease. The results from their study were recently published in *JAMA Oncology*.

The investigators created a model of prostate cancer incidence and mortality and developed it as part of the National Cancer Institute’s Cancer Intervention and Surveillance Modeling Network Prostate Cancer Working Group. A simulated contemporary cohort of US men beginning at 40 years of age underwent 18 strategies for PSA screening (see Figure). Treatment strategies included (1) contemporary treatment practices based on age and cancer stage and grade observed in the Surveillance, Epidemiology, and End Results program in 2010 or (2) selective treatment practices whereby cases with a Gleason score (a system of grading prostate cancer tissue based on how it looks under a microscope) lower than 7 and clinical T2a stage (the cancer is in one half or less of only one side of your prostate) cancer or lower are treated only after clinical progression, and all other cases undergo contemporary treatment practices. They analyzed national and trial data on PSA growth, screening and biopsy patterns, incidence of prostate cancer, treatment distributions, treatment efficacy, mortality, health-related quality of life, and direct medical expenditure. Data were collected from March 18, 2009 to August 15, 2014, and analyzed from November 20, 2012 to December 11, 2015.

Using the model, the investigators examined the following measures and outcomes: life-years (LYs), quality-adjusted life-years (QALYs), direct medical expenditure, and cost per LY and QALY gained. All 18 screening strategies were associated with increased LYs (range, 0.03-0.06) and costs ($263- $1,371) compared with no screening, with the cost ranging from $7,335 to $21,649 per LY. With contemporary treatment, only strategies with biopsy referral for PSA levels higher than 10.0 ng/mL or age-dependent thresholds were associated with increased QALYs (0.002-0.004), and only quadrennial screening of patients aged 55 to 69 years was potentially cost-effective in terms of cost per QALY (incremental cost-effectiveness ratio, $92,446). With selective treatment, all strategies were associated with increased QALYs (0.002-0.004), and several strategies were potentially cost-effective in terms of cost per QALY (incremental cost-effectiveness ratio, $70,831-$136,332).
"This study is important because it shows that when it comes to PSA screening, less is more," Dr. Roth states. In addition, "more conservative PSA screening strategies (that is, those with less frequent screening and higher PSA level thresholds for biopsy referral) are more likely to be cost-effective versus less conservative strategies. Additionally, we found that no strategy was likely to be of high value under contemporary treatment patterns where many men with low-risk prostate cancer (that is, those with a Gleason score lower than 7 and clinical T2a stage cancer or lower) receive treatment with surgery or radiation therapy, but several strategies were likely to be of at least moderate value with increased use of conservative management (that is, treating only after clinical progression) for low-risk, screen-detected cancers."

According to Dr. Roth, "Future studies should evaluate the feasibility and comparative effectiveness of personalized screening strategies, and additional cost-effectiveness analyses should be conducted to evaluate if they offer good value. For example, current work by study authors is exploring tailoring screening based on BRCA germline status, which has been associated with elevated risk of prostate cancer." Dr. Roth elaborates, "more personalized prostate cancer screening strategies are needed to tailor screening approaches to individual patients and further improve benefit-risk balance. By that, I mean rather than using a 'one size fits all' approach to screening, strategies should increasingly determine screening frequency, biopsy thresholds, and prostate cancer treatment approaches based on the specific characteristics of individual patients."

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