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Optimizing Prostate Cancer Surveillance: Using Data-driven Models for Informed Decision-making

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Current surveillance strategies in clinical practice are remarkably variable, and adherence to guideline recommendations—whether because of patient or provider factors—is quite low [1]. Given the low rates of metastatic progression and death in low-risk prostate cancer, prospective testing of different surveillance strategies against long-term oncologic endpoints is virtually impossible. Other approaches are needed to help lead the way forward. In this issue of *European Urology*, Sathianathen et al. [2] report results of a cost-effectiveness analysis for active surveillance strategies that use multiparametric magnetic resonance imaging (mpMRI) to compare the impact of biopsy-based and mpMRI-based surveillance strategies on both cost and quality-adjusted life years (QALYs).

With an abundance of data now confirming the safety of active surveillance in low-risk prostate cancer, the question is no longer one of whether surveillance should be the preferred management option but of how it should be implemented. The study by Sathianathen et al. [2] uses data-driven models for assessment of mpMRI, which the authors show has the potential to reduce harm from biopsies while still potentially minimizing delays in the detection of high-risk prostate cancer. Sathianathen et al. [2] used a Markov model to simulate the natural history of a hypothetical cohort of 50-yr-old men with newly diagnosed low-risk cancer. The authors evaluated the relative change in QALYs and cost according to several strategies varying in the frequency of biopsy (eg, annually, biennially, every 3 yr) and use of mpMRI. The resulting analysis provides evidence that MRI-based surveillance strategies could be cost-effective if key assumptions hold.

This study comes at a time when there are many open questions about the tradeoffs between overly intensive surveillance and delayed recognition of biopsy misclassification or progression. Here, Sathianathen and colleagues [2] present a new model that contributes to other recently developed models for patients on active surveillance. For example, Coley et al. [3] published an earlier model based on a Bayesian hierarchical model for predicting a latent health state from longitudinal clinical measurements. Our team also recently published a model using the same data, from the Johns Hopkins active surveillance study, but with different assumptions [4]. The Coley model assumed that patients could be misclassified due to biopsy undersampling, but assumed that no progression occurs. Our published model assumed that misclassification and progression from low- to high-risk cancer could occur. These models and others (eg, [5]) use differing but plausible models of the natural history of low-risk prostate cancer. Critically, results from each of these studies—including the present one—are dependent on the assumptions made. Here, for example, assumptions around rates of misclassification (estimated at 18.8%), MRI costs, treatment (prostatectomy only), and cure rates (extremely favorable) could all be questioned, although sensitivity analyses for many of these were reassuring.

The use of statistical models to compare active surveillance strategies is becoming increasingly important as mpMRI and other technologies are implemented largely on the basis of short-term data in this setting. This includes a broad set of serum, urine, and tissue biomarkers to go along with advanced imaging modalities that can potentially

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improve active surveillance by reducing the burden of biopsy and other health services imposed on patients. The work by Sathianathen et al. is particularly timely because of the significant discussion and debate over the use of mpMRI, which remains quite expensive in the USA and is still subject to wide variability in quality. Conversely, despite an expanding field of commercially available molecular biomarkers, none have shown utility for serial monitoring in active surveillance patients to date [6]. More observational biomarker and imaging studies are coming; yet, by necessity, nearly all will utilize the surrogate endpoint of biopsy upgrading.

The rapidly changing landscape of surveillance increases the need for data-driven models that look further into the future, which then raises the question of which model is best. A single ideal model cannot be identified because such a determination would require a single gold-standard data set. Variation across patient cohorts and uncertainty or ambiguity about the "right" model assumptions make the most practical approach one in which the goal is to determine multiple plausible models. This diversity of approaches will provide more robust recommendations that hedge against modeling errors, paralleling prior work related to prostate cancer screening [7].

The study by Sathianathen and colleagues appropriately follows commonly accepted practices for cost-effectiveness analysis, which focuses on the population perspective regarding average benefit and average cost relative to alternative options. The study serves the policy perspective well but does not guide patients and urologists on individual patient decisions after a new cancer diagnosis. Such guidance would need to incorporate at minimum a behavioral aspect of the patient decision-making process, specifically patients' preferences, something that is not captured by standard cost-effectiveness models. Patient preference is a particularly important aspect of active surveillance owing to the high variation in patient preferences for varying attributes of surveillance, which may partly explain poor adherence to active surveillance recommendations and relatively high rates of treatment in the absence of objective progression.

The cost-effectiveness analysis presented in this excellent study is an important first step to understanding the population perspective when it comes to the benefits and costs of using MRI for active surveillance. However, there is a need to move beyond crude measures of cost and QALYs, because they are not sufficient to capture the very personal nature of the decision that an individual man must make when contemplating active surveillance. Patient preference is of paramount importance in the context of active surveillance [8]. Therefore, there is a need to understand how factors such as risk sensitivity, perceived burden of surveillance versus definitive treatment, recommendations by a urologist, and input from patients' social networks may affect the decision to initiate and continue on active surveillance. Ultimately, a better understanding of how these and other potential factors influence patient preferences could guide the design of personalized strategies and potentially improve adherence to active surveillance.

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