

EDITORIAL COMMENT



Accurate pretreatment risk stratification plays a central role in optimizing management decisions for patients with clinically-localized prostate cancer. Nonetheless, the current approach to initial risk stratification is rapidly evolving, as novel tools such as tissue-based genomic assays are introduced.¹ While an ideal biomarker would be highly sensitive, specific, cost-effective, quantifiable, and reproducible, clinical tests often fall short of this standard.² As such, it is critical to establish the situational utility of emerging modalities in order to employ them efficiently and appropriately.

Based on a prospective multi-institutional study of the Oncotype DX Genomic Prostate Score (GPS), the authors report a prespecified subanalysis demonstrating that GPS provides both prognostic information and decisional reassurance to patients with favorable-risk prostate cancer electing surgery. First and foremost, the authors should be commended for their approach to this important question; prospective studies provide the optimal assessment of new clinical biomarkers but remain the exception in this space. At the same time, unanswered questions highlight the difficulty of conducting a truly definitive study of this type. For 1, how do we know that similar improvements in decisional conflict could not have been achieved through the use of free, publicly-available decision aids?³ Furthermore, as the authors acknowledge, the current report does not include men who elected active surveillance. While men electing treatment could be expected to experience some level of relief after simply making this decision, the more pertinent question may be how GPS impacts patients pursuing a less definitive, more anxiety-associated approach such as surveillance.⁴

It is also important to consider the manner in which biomarker data are reported. Odds ratios (OR) are traditionally used to convey the magnitude of associations, but, importantly, can vary greatly based on units and observed clinical range.⁵ While the current study reports an OR of 2.2 per 20 GPS units and a GPS range of 8-82, it is difficult to capture the clinical significance of the OR without a clear illustration of the overall GPS distribution. Furthermore, as illustrated by Pepe et al,⁵ ORs traditionally considered strong in the research setting are not adequate for discriminating between subjects who do and do not

experience the outcome at the individual level. One challenge of prognostic tests that report on a continuum of risk is the lack of a clear, singular threshold that can rule in or out the projected outcome.⁶ Moving forward, it may be useful for authors to additionally report threshold values with very high specificity and sensitivity observed in the study population. Clinical utility in this setting will continue to be challenged by a need to identify such thresholds for reliable, individual-level decision making.

Ultimately, the current study provides important prospective data while also drawing attention to the difficulties inherent to furthering our understanding of prostate cancer biomarkers. Additional studies will help to clarify the optimal clinical scenarios for implementing this test and others in this rapidly-evolving arena.

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