Genomic Classifiers and Prognosis of Localized Prostate Cancer: A Systematic Review

Matthew Boyer (matthew.boyer@duke.edu)
Duke University School of Medicine https://orcid.org/0000-0002-8970-2046

David Carpenter
Duke University School of Medicine https://orcid.org/0000-0002-9261-7168

Jeffrey Gingrich
Duke Cancer Institute, Center for Prostate & Urologic Cancers https://orcid.org/0000-0002-4516-2893

Sudha Raman
Duke University School of Medicine

Deepika Sirohi
University of Utah School of Medicine

Amir Alishahi Tabriz
Moffitt Cancer Center

Alexis Rompre-Brodeur
McGill University https://orcid.org/0000-0001-8177-0514

Joseph Lunyera
Duke University School of Medicine

Fahmin Basher
Duke University School of Medicine

Rhonda Bitting
Durham VA Health Care System

Andrezj Kosinski
Duke University School of Medicine

Sarah Cantrell
Duke University School of Medicine

Adelaide Gordon
Durham VA Health Care System

Belinda Ear
Durham VA Health Care System

Jennifer Gierisch
Durham VA Health Care System

Morgan Jacobs
Durham VA Health Care System

Karen Goldstein

Durham VA Health Care System

Article

Keywords:

Posted Date: September 6th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3296899/v1

Additional Declarations: There is **NO** conflict of interest to disclose.

Version of Record: A version of this preprint was published at Prostate Cancer and Prostatic Diseases on January 10th, 2024. See the published version at https://doi.org/10.1038/s41391-023-00766-z.

Abstract

Background

Refinement of the risk classification for localized prostate cancer is warranted to aid in clinical decision making. A systematic analysis was undertaken to evaluate the prognostic ability of three genomic classifiers, Decipher, GPS, and Prolaris, for biochemical recurrence, development of metastases and prostate cancer specific mortality in patients with localized prostate cancer.

Methods

Data Sources: MEDLINE, Embase, and Web of Science were queried for reports published January 2010 to April 2022.

Study Selection: Prospective or retrospective studies reporting prognosis for patients with localized prostate cancer.

Data *Extraction*: Relevant data were extracted into a customized database by 1 researcher with a second over reading. Risk of bias was assessed using a validated tool for prognostic studies, Quality in Prognosis Studies (QUIPS). Disagreements were resolved by consensus or by input from a third reviewer. We assessed certainty of evidence by GRADE incorporating adaptation for prognostic studies.

Results

Data Synthesis: A total of 39 studies (37 retrospective) involving over 10 000 patients were identified. Twenty-two assessed Decipher, 5 GPS, and 14 Prolaris. Thirty-four studies included patients who underwent prostatectomy. Based on very low to low certainty of evidence, each of three genomic classifiers modestly improved upon the prognostic ability for biochemical recurrence, development of metastases, and prostate cancer specific mortality compared to standard clinical risk classification schemes

Limitations: Downgrading of confidence in the evidence stemmed largely from bias due to the retrospective nature of the studies, heterogeneity in treatment received, and era in which patients were treated (i.e., prior to 2000s).

Conclusions:

Genomic classifiers provide a small but consistent improvement upon the prognostic ability of clinical classification schemes which may be helpful when treatment decisions are uncertain. However, definitive evidence from current management-era data is needed.

INTRODUCTION

Prostate cancer is the most common malignancy in men with an estimated 268,490 new cases in the United States in 2022, approximately 70% of whom will present with localized disease (1). To date, risk stratification to define prognosis and guide treatment has been based on clinical features such as prostate specific antigen (PSA) level and tumor staging (2). However, there is variability in patient outcomes not otherwise explained by currently recognized risk factors.

Tissue-based genomic classifier tests have been developed to refine the clinically based classification schemas and inform personalized recommendations for treatment. Three of the currently commercially available genomic classifier tests are Decipher, Genomic Prostate Score (formerly Oncotype DX GPS, hereafter referred to as GPS), and Prolaris. Each test provides a score based on the expression of a derived panel of genes in a patient's biopsy or prostatectomy specimen that can be used to estimate prognosis (3–5) (see test characteristics in Appendix Table 1). While large prospective studies are underway to assess the predictive ability of at least 1 of these tests (6, 7), results are not likely to be available for a decade or more. Meanwhile, a review of the prognostic ability of genomic classifier tests beyond clinical risk classification schemas for localized prostate cancer is needed to inform interim guidance for clinical care.

Table 1
Certainty of Evidence for Genomic Tests and Biochemical Recurrence, Metastasis, and Prostate Cancer–Specific Mortality

Outcome	Number of Studies	Findings	Certainty of Evidence (Rational)
Decipher			
Biochemical recurrence	4 observational studies (525 patients)	HR range (0.32 to 1.36) AUC range clinical features (0.56, 0.64) AUC range clinical features and genomic test (0.69 to 0.85)	**Low certainty** (downgraded for serious risk of bias and serious imprecision)
Metastases	15 observational studies (3,165 patients)	HR range (1.17 to 61.6) OR range (1.36, to 1.48) AUC range clinical features (0.46 to 0.88) AUC range clinical features and genomic test (0.67 to 0.89)	**Low certainty** (downgraded for serious risk of bias and serious indirectness)
Prostate cancer–specific mortality	5 observational studies (1,807 patients)	HR range (1.39 to 56.0) OR range (1.20) AUC range clinical features (0.55 to 0.81) AUC range clinical features and genomic test (0.71 to 0.78)	**Low certainty** (downgraded for serious indirectness and serious imprecision)
Oncotype			

Abbreviations: AUC = area under the curve; OR = odds ratio; HR = hazard ratio

Outcome	Number of Studies	Findings	Certainty of Evidence (Rational)
Biochemical recurrence	3 observational studies (876 patients)	HR range (1.10 to 2.73) AUC range clinical features (0.59) AUC range clinical features and genomic test (0.68)	**Very low certainty** (downgraded for serious inconsistency, serious indirectness, and serious imprecision)
Metastases	3 observational studies (793 patients)	HR range (2.24 to 2.63) AUC range clinical features (0.55 to 0.77) AUC range clinical features and genomic test (0.65 to 0.824)	**Very low certainty** (downgraded for serious risk of bias, serious indirectness, and serious imprecision)
Prostate cancer–specific mortality	3 observational studies (847 patients)	HR range (2.69, 2.30) AUC range clinical features (0.55 to 0.762) AUC range clinical features and genomic test (0.69 to 0.822)	**Very low certainty** (downgraded for serious risk of bias, serious indirectness, serious imprecision)
Prolaris			
Biochemical Recurrence	9 observational studies (2,758 patients)	HR range (1.24 to 10.9) AUC range clinical features (0.542 to 0.78) AUC range clinical features and genomic test (0.65 to 0.86)	**Very low certainty** (downgraded for very serious risk of bias, serious indirectness, serious imprecision, and suspected publication bias)

Abbreviations: AUC = area under the curve; OR = odds ratio; HR = hazard ratio

Outcome	Number of Studies	Findings	Certainty of Evidence (Rational)
Metastases	4 observational studies (2,571 patients)	HR range (2.05 to 4.19) AUC range clinical features (0.55 to 0.894) AUC range clinical features and genomic test (0.90) Test only (0.73)	**Very low certainty** (downgraded for serious risk of bias, serious inconsistency, serious indirectness, and serious imprecision)
Prostate cancer–specific mortality	3 observational studies (1,989 patients)	HR range (1.65 to 2.57) AUC range clinical features (0.74, 0.55) AUC range clinical features and genomic test (0.78) AUC test only (0.66)	**Very low certainty** (downgraded for serious risk of bias, serious inconsistency, very serious indirectness, and serious imprecision)
Abbreviations: AUC = area under the curve; OR = odds ratio; HR = hazard ratio			

METHODS

Study Design

This work is part of a Veterans Health Administration (VHA)-funded Evidence Synthesis Program report (www.hsrd.research.va.gov/publications/esp). The Evidence Synthesis Program is a partnered program in the Department of Veterans Affairs (VA) which conducts systematic reviews on topics of prioritized relevance to VA operational partners. We work with operations partners to refine the review question, obtain clinical context; however the partners are not involved in conducting the review. We also convened a technical expert panel for additional clinical input. We developed and followed a standard protocol for this review which was registered publicly (PROSPERO:CRD42022347950) and followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidance (8).

Data Sources and Searches

MEDLINE (via Ovid), Embase (via Elsevier), and Web of Science (via Clarivate) databases were searched for references published from January 2010 to April 2022 using a combination of database-specific controlled vocabulary terms and keywords developed by a medical librarian and study authors. The search strategies were peer reviewed by another librarian using a modified PRESS checklist (9). The

searches were conducted on April 24, 2022 (Search strategies are presented in Appendix Table 2). In addition, we hand-searched previous systematic reviews conducted on this or a related topic for relevant studies and solicited additional citations from the topic nominators and our technical expert panel.

Study Selection

Eligibility criteria included manuscripts published in a peer-reviewed journal that assessed the prognostic ability of the Decipher, GPS, or Prolaris genomic classifiers for clinical outcomes of patients with localized prostate cancer who have undergone definitive surgery and/or radiation as compared to clinical risk stratification models. Key exclusion criteria included patients with metastatic disease, use of other genomic tests, and adverse pathology as the sole reported outcome. Full eligibility criteria are described in Appendix Table 3. Studies identified through our search were independently reviewed based on title and abstract by 2 investigators. All citations marked for inclusion by at least 1 investigator were reviewed at full-text level. Citations designated for exclusion by 1 investigator at the title and abstract level underwent screening by a second investigator. If both investigators agreed on exclusion, the study was excluded. All articles meeting eligibility criteria at full-text review were included for data extraction. Citations were tracked in an electronic database (for referencing, EndNote, Clarivate Analytics, Philadelphia, PA; for data abstraction, DistillerSR, Evidence Partners Inc., Manotick, ON, Canada).

Data Extraction and Quality Assessment

Included reports were extracted into a customized DistillerSR database by 1 reviewer and over-read by a second. Disagreements were resolved by consensus or by obtaining a third reviewer's opinion. Our extraction process was guided by CHARMS-PF (the checklist for critical appraisal and data extraction for systematic reviews of prognostic factor studies) (10). In accordance with our *a priori* plan, we prioritized randomized trials, prospective cohort studies, cohorts with longer follow-up duration (> 5 years), nested case-control studies, and validation or confirmatory studies over training cohorts or data used to establish a test, given the volume of identified literature.

For survival and other time-to-event outcomes, we extracted hazard ratios and corresponding 95% confidence intervals (CIs). We prioritized extraction of the most adjusted prognostic effect estimates. We considered a minimum set of established prognostic factors (*ie*, PSA, Gleason score, and clinical tumor [T] stage) for adequate adjustment. When studies reported multiple models using different approaches to adjusting for clinical risk factors (*eg*, NCCN vs CAPRA risk stratification models, individual clinical risk factors), we prioritized the use of models as follows: 1) for cohorts with an intact prostate and who had *not* received definitive therapy, we prioritized models using NCCN risk categorization, followed by CAPRA, and then individual clinical features; 2) for post radical prostatectomy patients, we prioritized CAPRA-S, followed by models with individual clinical risk factors.

We used the validated "Quality in Prognosis Studies" tool (QUIPS) to assess risk of bias (ROB)in prognostic factor studies (11). QUIPS criteria include domains such as adequacy of randomization and allocation concealment, comparability of groups at baseline, completeness of follow-up and differential loss to follow-up. Based on a previously published approach, any study that was rated high in 1 or more

domains or moderate for 3 or more was considered high ROB overall and any study that was rated low ROB in all 6 domains or up to 1 moderate ROB was considered low ROB overall (12). Studies that did not meet either of those conditions were considered moderate ROB overall. ROB assessment was initially completed in duplicate for 25% of included studies. Because we found sufficient agreement, the remaining included studies were assessed for ROB by 1 investigator and over-read by a second given the volume of included studies. Lastly, we audited ROB assessments for consistency across all included studies.

Data Synthesis and Analysis

We summarized key study characteristics of the primary literature for each test type separately. We did not combine outcomes across the 3 genomic classifier tests, as each evaluates a distinct and non-equivalent gene panel.

When feasible based on the volume of literature, types of effect measures reported, and completeness of results, we conducted a quantitative synthesis (*ie*, meta-analysis) to estimate summary prognostic effects. Effect estimates were grouped by outcome, statistical effect measure, time point of outcome measurement, and conceptual consistency. Conceptual consistency was primarily based on clinical context (*eg*, those who had received or not received definitive initial treatment for prostate cancer). We grouped outcomes by time point of measurement (eg, 3–5 years after test measurement vs 6–10 years) due to the current understanding of the natural history of prostate cancer. For time-to-metastasis or metastasis-free survival, we combined studies by distant and/or regional metastases. This decision was driven by the recognition that while the location of metastases can drive treatment decisions, attention to the location of metastases has evolved over the time span of many included studies. Because the genomic classifier tests of interest are reported as both a continuous variable and a categorical variable, we report both. We aggregated outcomes only when there were at least 3 studies with the same outcome.

Random-effects models were used for meta-analyses; we also used the Knapp-Hartung approach to better account for uncertainty in estimates of the amount of heterogeneity among studies as all included fewer than 20 studies. For meta-analysis which were based on different numbers of score unit increases, the HRs and 95% CIs were adjusted to correspond to a 20-unit increase. We evaluated heterogeneity using visual inspection of forest plots and 95% prediction intervals. When a quantitative synthesis was not feasible, we summarized the data narratively. We gave more weight to the evidence from higher quality studies with more precise estimates of effect.

Certainty of Evidence

We assessed certainty of evidence using GRADE with consideration of guidance around adaptation for prognostic studies including not downgrading for observational study designs (13). In brief, this approach requires assessment of 4 domains: ROB, consistency, directness, and precision. We assigned a summary rating of high, moderate, low, or very low certainty of evidence based on consensus among 3 investigators (KG, MB, AG). Studies that included patient data from the 1980s or early 1990s were

downgraded for indirectness because patients in these studies have limited comparability with patients receiving modern cancer screening and treatment.

Role of the Funding Source

The US Department of Veterans Affairs was not involved in the design, conduct, or analysis interpretation.

RESULTS

1 573 unique articles were initially identified. After applying eligibility criteria to titles and abstracts, 145 articles remained for full-text review. Of these, 39 were included and retained for data abstraction for the full report. These studies included more than 10,000 patients and addressed the prognostic utility of incorporating genomic classifiers into clinical risk-classification schemes (3, 5, 14–51) (see Appendix Fig. 1).

Twenty-two studies assessed Decipher, 5 GPS, and 14 Prolaris, with 1 study investigating all 3 genomic classifiers (16). Seven studies compared the prognostic ability of the genomic classifier to NCCN risk classification, 22 to CAPRA or CAPRA-S, 1 to AUA, and 24 to a combination of clinical features unique to the study. A plurality of studies reported multiple comparisons across clinical risk-classification schemes. Sixteen retrospective studies investigated biochemical recurrence, 20 the rate of metastases, and 10 prostate-cancer-specific mortality. Five studies included composite endpoints, of which 2 were prospective and the remaining 3 retrospective. Twenty-four studies ran the genomic classifier on prostatectomy tissue (3, 15–22, 27, 28, 31, 34, 37–40, 42, 43, 45, 47, 50, 51), 20 on biopsy tissue (5, 14, 18, 19, 22–26, 29, 30, 32, 35, 36, 38, 41, 44, 46, 48, 50), and 5 on a combination of the two (18, 19, 22, 38, 50). Twenty-six studies included patients diagnosed prior to 2000 (3, 5, 15–17, 19, 20, 22, 28–34, 37, 38, 40–44, 46–48, 50), and 9 included patients diagnosed prior to 1990 (3, 5, 15, 20, 31, 32, 38, 43, 48). One study did not report the timeframe from which the patients were drawn, while another reported patients diagnosed prior to 2017 (18, 26). The majority of studies, 34, included patients who initially underwent prostatectomy. Nine studies included patients who were treated with definitive radiation with only 3 studies including patients that solely received definitive radiation (14, 19, 22, 24, 25, 29, 32, 35, 46). Two studies did not report the treatments received (41, 48). Across studies, there was substantial variability in the clinical risk-classification models, outcome of interest, and statistical measure used to assess the impact of the genomic classifier. For complete study characteristics, see Appendix Table 4.

Common risks of bias among included studies were exclusion of potentially eligible participants due to insufficient tissue sample or tissue quality, exclusion of patients lost to follow-up who might have had adverse outcomes, inadequate adjusting for confounders, limited follow-up duration, and lack of details about missing data. Less common was having the genomic classifier test run by a lab other than the commercial lab. Eighteen studies were found to have low ROB (3, 5, 14, 15, 17, 19, 20, 22, 24, 26, 30, 39, 41–45, 47), 11 moderate ROB (23, 28, 31, 34, 35, 37, 38, 40, 46, 48, 51), and 10 high ROB (16, 18, 21, 25, 27, 29, 33, 36, 50) (see Appendix Fig. 2). Of note, 17 studies appear to have been sponsored or co-authored by the commercial companies with rights to the genomic classifier tests under study.

Biochemical Recurrence

Sixteen retrospective studies reported the key outcome of biochemical recurrence, either an absolute rise to 0.2 ng/ml following prostatectomy or a relative rise to 2 ng/ml above the nadir following radiation. Genomic classifiers showed a modest but consistent improvement in prediction of BCR in either setting. Four studies evaluated the additional benefit of the Decipher score (18, 25, 35, 39), three GPS (23, 30, 44), and nine Prolaris (3, 21, 26, 27, 33, 36, 46, 47, 50). Three studies were undertaken in patients who underwent definitive radiation while the remaining were post prostatectomy. The summary estimate HR for BCR across 3 studies evaluating the Decipher score as a continuous variable was 1.20 (95% CI [1.00, 1.43]; 95% prediction interval [PI] [1.00, 1.43), indicating a 20% increase in the risk of BCR with per unit increase in Decipher score than when clinical classification schemes were considered alone. The summary estimate HR for GPS across 3 studies was 2.03 (95% CI [0.93, 4.45); 95% PI [0.54, 7.66]). The summary estimate HR across the Prolaris studies was 1.44 (95% CI [1.28, 1.62]; 95% PI [1.28, 1.62]). Effect estimates for biochemical recurrence are summarized in Fig. 1.

Metastases

Twenty studies addressed the predictive ability of genomic classifiers for development of metastases. One of these studies investigated all three genomic classifiers reporting AUCs of 0.74, 0.65, and 0.73 for the Decipher, GPS, and Prolaris scores, respectively, in models with PSA, T stage, and Grade Group compared to 0.55 with those clinical characteristics alone (16). Fifteen studies analyzed the ability of the Decipher score to predict metastases following definitive treatment of prostate cancer, including 14 retrospective studies and 1 secondary analysis of a prospective, randomized trial (5, 17, 19, 20, 25, 28, 29, 32, 35, 37, 38, 40, 42, 43). The number of metastatic events in these studies were low, ranging from 5 to 104. Across 9 studies, the summary effect estimate showed an increase in risk of metastases with continuous increase in Decipher score with an HR of 1.32 (95% CI [1.22, 1.44]; 95% PI [1.15, 1.52]). The ancillary analysis of a subset of patients in a phase III prospective randomized trial evaluating the addition of 2 years of ADT to post-prostatectomy radiation (RTOG 9601) reported an improvement in prognostic ability with a HR of 1.17 (95% CI [1.05 to 1.32]), however, was underpowered to detect a statistically significant interaction between the Decipher score and the effect of ADT(17). Decipher score as a continuous measure is summarized in Fig. 2a and as a categorical measure in Fig. 2b.

Two retrospective studies reported HRs of 2.24 and 2.34 supporting the additive value of GPS to predict development of metastases when combined with standard clinical features. Across 3 retrospective studies of Prolaris, the summary effect estimate showed a HR of 2.34 (95% CI [1.12, 4.90]; 95% PI [0.83, 6.58]). The predictive ability of GPS and Prolaris for development of metastases are summarized in Fig. 2a.

Prostate Cancer–specific Mortality

Ten studies assessed test prognostic ability for prostate cancer specific mortality. The same study which examined all three tests showed AUCs of 0.72, 0.69, and 0.66 for Decipher, GPS, and Prolaris, respectively,

and clinical features compared to 0.55 for clinical features alone (16). Four studies (17, 20, 31, 45) investigated the impact of the Decipher score on the prediction of prostate-cancer-specific mortality in addition to standard clinical or pathologic features. One study reported a HR of 56 (95% CI 6.82–7297) likely due to the small number of events (n = 20) and a model that included the Decipher score as a categorical variable (20). The other studies reported HRs of 1.39 and 1.81 with one reporting an OR of 1.34. The ancillary analysis of RTOG 9601 showed the prognostic ability of the Decipher score for overall survival, with an HR of 1.17 (95% CI [1.06, 1.29]) in a model similar to those for prostate-cancer-specific mortality (17).

Two studies reported the HRs for prostate-cancer-specific mortality with GPS testing, 2.69 (95% CI [1.50, 4.82]) in a model with NCCN (30) and 2.30 (95% CI [1.45, 4.36]) in a model with clinical features (15). Three Prolaris studies reported a summary HR of 1.72 (95% CI [1.58, 1.87]; 95% PI [1.58, 1.87]). Studies addressing prostate cancer specific mortality are summarized in Fig. 3.

Other Outcomes

Three additional studies assessed alternative or composite endpoints with Decipher testing (14, 34, 39, 51). A study of 241 patients treated with definitive radiation or prostatectomy were evaluated for time-to-treatment failure defined as biochemical recurrence or initiation of salvage therapy after definitive treatment (14). The HR for time to treatment failure was 2.98 (95% CI [1.22, 7.29]) in a model containing NCCN risk classification and other clinical features. A study using Decipher reported clinical recurrence (noted to be distinct from biochemical recurrence but not clearly defined) was found to have an HR of 1.48 (95% CI [1.09, 2.01]) in a model with CAPRA-S.(39). A second study assessed the composite endpoint of time to clinical recurrence after prostatectomy and found that Decipher as a categorical variable had HRs of 1.40 (95% [CI 0.7, 2.74]) and 2.93 (95% CI [1.58, 5.55]) for intermediate and high risk scores, respectively, in a model with clinical features (34). Lastly, time to secondary therapy was reported after radical prostatectomy for Decipher with a HR of 1.46 (1.34 to 1.66) in a model with clinical features (51). No studies with GPS were identified that evaluated other endpoints. One retrospective Prolaris study reported a composite endpoint of metastasis or prostate-cancer-specific mortality after prostatectomy in a model including CAPRA-S and Prolaris scores with an HR of 2.15 (95% CI [1.36, 3.39])(26). These results are summarized in Appendix Fig. 3.

Certainty of Evidence

Overall, we note that while the effect estimates were consistent in showing a clinically relevant additive benefit of the genomic tests, our certainty of evidence (COE) assessments were frequently downgraded for issues related to indirectness reflecting the era from which the data were drawn. For Decipher, we have low COE that this test provides additional prognostic information for risk of BCR, metastases, and prostate cancer–specific mortality. For GPS, we have very low COE across all 3 outcomes. For Prolaris, we have very low COE across all 3 outcomes. See Table 1 for additional details and reasons for downgrading of each outcome by test type.

DISCUSSION

Based on 39 studies, three genomic classifiers for localized prostate cancer (Decipher, GPS, and Prolaris) modestly improve upon the prognostic ability of currently employed clinical classification schemes. For studies evaluating the genomic classifier scores as continuous variables, the hazard ratios across clinical outcomes including biochemical recurrence, development of metastases, and prostate cancer specific mortality, ranged from 1.16–2.05 for Decipher, 1.10–2.73 for GPS, and 1.24–4.19 for Prolaris. The magnitude and clinical meaning of this improvement is, however, called into question by the low (Decipher) or very low (Prolaris and GPS) certainty of evidence of these studies.

Overall, our findings are largely consistent with prior reviews on this topic. Specifically, six recent reviews examined 1 or more of our 3 outcomes of interest (52–57). Two systematic reviews examined only the Decipher test (55, 57). As with our findings, each review noted that genomic classifier tests modestly improve clinical outcome prediction compared to clinical features alone. A few earlier reviews summarized the results of this rapidly changing field but did not employ standard systematic review methodology such as including a formal risk of bias assessment (52, 58). Our review adds to prior reviews by adding a significant number of studies, more recent studies (an additional 12 articles since the last review's search period), formal risk of bias and certainty of evidence assessment for all included studies, and exploration of test effects by key subgroups. In addition, we defined a standard set of expected risk factors for adjustment across analytic models to account for key clinical factors (ie, PSA, Gleason score, and clinical tumor [T] stage).

A key contributing factor to the low or very low certainty of evidence for our findings stems from many patients contributing data to included articles receiving care during an older management era. Twenty-six of the 39 studies identified included patients diagnosed prior to 2000 and nine included those diagnosed prior to 1990. Since those earlier eras, the detection and management of prostate cancer has evolved significantly. More recent advancements include the incorporation of PSA in screening (59), evolving imaging modalities including MRI and PET (60), dose escalated, image guided radiation with or without androgen deprivation therapy (61), and robot assisted prostatectomy (62). It is unclear how the findings from this review would change if the evaluations were repeated with data solely from patients receiving contemporary care. Ongoing prospective studies in the setting of definitive radiation or surgery may provide further insight into the value of these tests in current practice.

In addition to the inclusion of older patient data, the existing evidence has other notable limitations. First, the clinical classification scheme employed as a comparator to the results of the genomic classifier was inconsistent. While we prioritized analyses including NCCN or CAPRA, we found that 16 of the 39 identified studies compared genomic classifiers to a combination of features, such as log(PSA), that would not typically be employed to determine prognosis in a clinical setting. In addition, the NCCN risk classification has changed over time and patients classified at a certain risk level retrospectively may not have been managed as they would be at present. Moreover, "low" risk by NCCN criteria does not correlate directly with "low" by Decipher despite identical terminology limiting comparison. Second, definitions and

measurement of key outcomes varied. Nine of the studies solely reported on the prognostic ability for biochemical recurrence which is a poor surrogate for overall survival and is not currently accepted as an endpoint for clinical trials (63). Notably, the bulk of the data for GPS and Prolaris tests used earlier endpoints such as biochemical recurrence, while Decipher was the predominantly studied with later or "harder" outcomes such as prostate cancer–specific mortality. It is possible that studies of GPS and Prolaris with longer-term outcomes have not been completed yet. We note that there are 4 Prolaris studies registered in clinicaltrials.gov that appear to have completed data collection but are without peer-reviewed publications or posted results (64–66) or were terminated due to poor enrollment (67). Finally, much of the identified literature was retrospective cohort studies from individual or grouped institutional data from previously treated patients; many of these were from the same institutions, as noted by multiple linked studies evaluating the same cohort data (3, 33, 38, 43, 48, 50). It is possible that data from these included studies may overlap substantially, although in some cases, the amount is unclear (29, 34, 37, 40, 42). It is possible other institutions may have conducted retrospective analyses which have gone unpublished.

Among the limitations of the present review is that our a priori criteria for conceptual heterogeneity may differ from those used by others when combining studies for calculating summary HRs. This review was also limited to reports published in full manuscript form thus may exclude more recent reports published in abstract version only. Additional studies have addressed the role of these genomic classifiers in other settings (eg, metastatic prostate cancer) or investigated other existing genomic classifiers (68–70), but which were not the focus of this review.

In conclusion, genomic classifiers for localized prostate cancer appear to augment the prognostic ability of clinical risk stratification schemes although the studies supporting this have a number of methodological limitations which must be considered when applying to the current management of prostate. Additional analyses are warranted incorporating modern clinical stratification, staging, and treatment to offer more direct and relevant evidence for application to the prostate cancer care we deliver today.

Declarations

Disclaimer: The views expressed are those of the authors and do not reflect the official views or policy of the U.S. Department of Defense or its components.

Acknowledgment: The authors thank the following key stakeholders and technical expert panel members for provided advice during the conduct of this review but who do not necessarily endorse the stated conclusions: Drs. Maria Kelly, Edward Obedian, Michael G. Chang, Andrew Armstrong, Daniel Spratt, and Jeremy Shelton. Additionally, we would like to thank Liz Wing and Stacy Lavin, for editorial assistance, and Julie Snyder for administrative support.

Financial Support: This project was funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative (ESP 09-010). This work was also supported by the Durham Center of

Innovation to Accelerate Discovery and Practice Transformation (ADAPT) (CIN 13-410) at the Durham VA Health Care System. Primary Funding Source: U.S. Department of Veterans Affairs (PROSPERO CRD42022347950)

Conflict of Interest: Authors declare no conflict of interest.

Availability of Data and Materials: Study protocol: Available at www.crd.york.ac.uk/prospero (PROSPERO: CRD42022347950). Statistical code and data set: Available from Ms. Gordon (e-mail, adelaide.gordon@va.gov).

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72(1):7–33.
2. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GA, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA. 1998;280(11):969–74.
3. Cuzick J, Swanson GP, Fisher G, Brothman AR, Berney DM, Reid JE, et al. Prognostic value of an RNA expression signature derived from cell cycle proliferation genes in patients with prostate cancer: a retrospective study. Lancet Oncology. 2011;12(3):245–55.
4. Knezevic D, Goddard AD, Natraj N, Cherbavaz DB, Clark-Langone KM, Snable J, et al. Analytical validation of the Oncotype DX prostate cancer assay - a clinical RT-PCR assay optimized for prostate needle biopsies. BMC Genomics. 2013;14:690.
5. Erho N, Crisan A, Vergara IA, Mitra AP, Ghadessi M, Buerki C, et al. Discovery and validation of a prostate cancer genomic classifier that predicts early metastasis following radical prostatectomy. PLoS One. 2013;8(6):e66855.
6. NRG Oncology 2023. Two Studies for Patients With High Risk Prostate Cancer Testing Less Intense Treatment for Patients With a Low Gene Risk Score and Testing a More Intense Treatment for Patients With a High Gene Risk Score, The PREDICT-RT Trial. Accessed at https://clinicaltrials.gov/ct2/show/NCT04513717 on January 16 2023.
7. NRG Oncology 2023. Two Studies for Patients With Unfavorable Intermediate Risk Prostate Cancer Testing Less Intense Treatment for Patients With a Low Gene Risk Score and Testing a More Intense Treatment for Patients With a Higher Gene Risk Score. Accessed at https://clinicaltrials.gov/ct2/show/NCT05050084 on January 16 2023.
8. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
9. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. J Clin Epidemiol. 2016;75:40–6.
10. Riley RD, Moons KGM, Snell KIE, Ensor J, Hooft L, Altman DG, et al. A guide to systematic review and meta-analysis of prognostic factor studies. Bmj. 2019;364:k4597.

11. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. Ann Intern Med. 2013;158(4):280–6.
12. Grooten WJA, Tseli E, Äng BO, Boersma K, Stålnacke BM, Gerdle B, et al. Elaborating on the assessment of the risk of bias in prognostic studies in pain rehabilitation using QUIPS-aspects of interrater agreement. Diagn Progn Res. 2019;3:5.
13. Iorio A, Spencer FA, Falavigna M, Alba C, Lang E, Burnand B, et al. Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients. Bmj. 2015;350:h870.
14. Vince RA, Jr., Jiang R, Qi J, Tosoian JJ, Takele R, Feng FY, et al. Impact of Decipher Biopsy testing on clinical outcomes in localized prostate cancer in a prospective statewide collaborative. Prostate Cancer & Prostatic Diseases. 2021;20:20.
15. Brooks MA, Thomas L, Magi-Galluzzi C, Li J, Crager MR, Lu R, et al. GPS Assay Association With Long-Term Cancer Outcomes: Twenty-Year Risk of Distant Metastasis and Prostate Cancer-Specific Mortality. JCO Precision Oncology. 2021;5.
16. Lehto TK, Sturenberg C, Malen A, Erickson AM, Koistinen H, Mills IG, et al. Transcript analysis of commercial prostate cancer risk stratification panels in hard-to-predict grade group 2–4 prostate cancers. Prostate. 2021;81(7):368–76.
17. Feng FY, Huang HC, Spratt DE, Zhao SG, Sandler HM, Simko JP, et al. Validation of a 22-Gene Genomic Classifier in Patients With Recurrent Prostate Cancer: An Ancillary Study of the NRG/RTOG 9601 Randomized Clinical Trial. JAMA Oncology. 2021;7(4):544–52.
18. Ramotar M, Chua MLK, Truong H, Hosni A, Pintilie M, Davicioni E, et al. Subpathologies and genomic classifier for treatment individualization of post-prostatectomy radiotherapy. Urologic Oncology. 2022;40(1):5.e1-5.e13.
19. Tosoian JJ, Birer SR, Jeffrey Karnes R, Zhang J, Davicioni E, Klein EE, et al. Performance of clinicopathologic models in men with high risk localized prostate cancer: impact of a 22-gene genomic classifier. Prostate Cancer & Prostatic Diseases. 2020;23(4):646–53.
20. Howard LE, Zhang J, Fishbane N, Hoedt AM, Klaassen Z, Spratt DE, et al. Validation of a genomic classifier for prediction of metastasis and prostate cancer-specific mortality in African-American men following radical prostatectomy in an equal access healthcare setting. Prostate Cancer & Prostatic Diseases. 2020;23(3):419–28.
21. Shangguan X, Qian H, Jiang Z, Xin Z, Pan J, Dong B, et al. Cell cycle progression score improves risk stratification in prostate cancer patients with adverse pathology after radical prostatectomy. Journal of Cancer Research & Clinical Oncology. 2020;146(3):687–94.
22. Canter DJ, Freedland S, Rajamani S, Latsis M, Variano M, Halat S, et al. Analysis of the prognostic utility of the cell cycle progression (CCP) score generated from needle biopsy in men treated with definitive therapy. Prostate Cancer & Prostatic Diseases. 2020;23(1):102–7.
23. Kornberg Z, Cooperberg MR, Cowan JE, Chan JM, Shinohara K, Simko JP, et al. A 17-Gene Genomic Prostate Score as a Predictor of Adverse Pathology in Men on Active Surveillance. Journal of

Urology. 2019;202(4):702–9.

24. Canter DJ, Reid J, Latsis M, Variano M, Halat S, Rajamani S, et al. Comparison of the Prognostic Utility of the Cell Cycle Progression Score for Predicting Clinical Outcomes in African American and Non-African American Men with Localized Prostate Cancer. European Urology. 2019;75(3):515–22.
25. Berlin A, Murgic J, Hosni A, Pintilie M, Salcedo A, Fraser M, et al. Genomic Classifier for Guiding Treatment of Intermediate-Risk Prostate Cancers to Dose-Escalated Image Guided Radiation Therapy Without Hormone Therapy. International Journal of Radiation Oncology, Biology, Physics. 2019;103(1):84–91.
26. Leapman MS, Nguyen HG, Cowan JE, Xue L, Stohr B, Simko J, et al. Comparing Prognostic Utility of a Single-marker Immunohistochemistry Approach with Commercial Gene Expression Profiling Following Radical Prostatectomy. European Urology. 2018;74(5):668–75.
27. Leon P, Cancel-Tassin G, Drouin S, Audouin M, Varinot J, Comperat E, et al. Comparison of cell cycle progression score with two immunohistochemical markers (PTEN and Ki-67) for predicting outcome in prostate cancer after radical prostatectomy. World Journal of Urology. 2018;36(9):1495–500.
28. Spratt DE, Dai DLY, Den RB, Troncoso P, Yousefi K, Ross AE, et al. Performance of a Prostate Cancer Genomic Classifier in Predicting Metastasis in Men with Prostate-specific Antigen Persistence Postprostatectomy. European Urology. 2018;74(1):107–14.
29. Spratt DE, Zhang J, Santiago-Jimenez M, Dess RT, Davis JW, Den RB, et al. Development and Validation of a Novel Integrated Clinical-Genomic Risk Group Classification for Localized Prostate Cancer. Journal of Clinical Oncology. 2018;36(6):581–90.
30. Van Den Eeden SK, Lu R, Zhang N, Quesenberry CP, Jr., Shan J, Han JS, et al. A Biopsy-based 17-gene Genomic Prostate Score as a Predictor of Metastases and Prostate Cancer Death in Surgically Treated Men with Clinically Localized Disease. European Urology. 2018;73(1):129–38.
31. Karnes RJ, Choeurng V, Ross AE, Schaeffer EM, Klein EA, Freedland SJ, et al. Validation of a Genomic Risk Classifier to Predict Prostate Cancer-specific Mortality in Men with Adverse Pathologic Features. European Urology. 2018;73(2):168–75.
32. Nguyen PL, Haddad Z, Ross AE, Martin NE, Deheshi S, Lam LLC, et al. Ability of a Genomic Classifier to Predict Metastasis and Prostate Cancer-specific Mortality after Radiation or Surgery based on Needle Biopsy Specimens. European Urology. 2017;72(5):845–52.
33. Tosoian JJ, Chappidi MR, Bishoff JT, Freedland SJ, Reid J, Brawer M, et al. Prognostic utility of biopsy-derived cell cycle progression score in patients with National Comprehensive Cancer Network low-risk prostate cancer undergoing radical prostatectomy: implications for treatment guidance. BJU International. 2017;120(6):808–14.
34. Dalela D, Santiago-Jimenez M, Yousefi K, Karnes RJ, Ross AE, Den RB, et al. Genomic Classifier Augments the Role of Pathological Features in Identifying Optimal Candidates for Adjuvant Radiation Therapy in Patients With Prostate Cancer: Development and Internal Validation of a Multivariable Prognostic Model. Journal of Clinical Oncology. 2017;35(18):1982–90.

35. Nguyen PL, Martin NE, Choeurng V, Palmer-Aronsten B, Kolisnik T, Beard CJ, et al. Utilization of biopsy-based genomic classifier to predict distant metastasis after definitive radiation and short-course ADT for intermediate and high-risk prostate cancer. Prostate Cancer & Prostatic Diseases. 2017;20(2):186–92.
36. Oderda M, Cozzi G, Daniele L, Sapino A, Munegato S, Renne G, et al. Cell-cycle Progression-score Might Improve the Current Risk Assessment in Newly Diagnosed Prostate Cancer Patients. Urology. 2017;102:73–8.
37. Ross AE, Den RB, Yousefi K, Trock BJ, Tosoian J, Davicioni E, et al. Efficacy of post-operative radiation in a prostatectomy cohort adjusted for clinical and genomic risk. Prostate Cancer & Prostatic Diseases. 2016;19(3):277–82.
38. Klein EA, Haddad Z, Yousefi K, Lam LL, Wang Q, Choeurng V, et al. Decipher Genomic Classifier Measured on Prostate Biopsy Predicts Metastasis Risk. Urology. 2016;90:148–52.
39. Glass AG, Leo MC, Haddad Z, Yousefi K, du Plessis M, Chen C, et al. Validation of a Genomic Classifier for Predicting Post-Prostatectomy Recurrence in a Community Based Health Care Setting. Journal of Urology. 2016;195(6):1748–53.
40. Ross AE, Johnson MH, Yousefi K, Davicioni E, Netto GJ, Marchionni L, et al. Tissue-based Genomics Augments Post-prostatectomy Risk Stratification in a Natural History Cohort of Intermediate- and High-Risk Men. European Urology. 2016;69(1):157–65.
41. Cuzick J, Stone S, Fisher G, Yang ZH, North BV, Berney DM, et al. Validation of an RNA cell cycle progression score for predicting death from prostate cancer in a conservatively managed needle biopsy cohort. British Journal of Cancer. 2015;113(3):382–9.
42. Den RB, Yousefi K, Trabulsi EJ, Abdollah F, Choeurng V, Feng FY, et al. Genomic classifier identifies men with adverse pathology after radical prostatectomy who benefit from adjuvant radiation therapy. Journal of Clinical Oncology. 2015;33(8):944–51.
43. Klein EA, Yousefi K, Haddad Z, Choeurng V, Buerki C, Stephenson AJ, et al. A genomic classifier improves prediction of metastatic disease within 5 years after surgery in node-negative high-risk prostate cancer patients managed by radical prostatectomy without adjuvant therapy. European Urology. 2015;67(4):778–86.
44. Cullen J, Rosner IL, Brand TC, Zhang N, Tsiatis AC, Moncur J, et al. A Biopsy-based 17-gene Genomic Prostate Score Predicts Recurrence After Radical Prostatectomy and Adverse Surgical Pathology in a Racially Diverse Population of Men with Clinically Low- and Intermediate-risk Prostate Cancer. European Urology. 2015;68(1):123–31.
45. Cooperberg MR, Davicioni E, Crisan A, Jenkins RB, Ghadessi M, Karnes RJ. Combined value of validated clinical and genomic risk stratification tools for predicting prostate cancer mortality in a high-risk prostatectomy cohort. European Urology. 2015;67(2):326–33.
46. Freedland SJ, Gerber L, Reid J, Welbourn W, Tikishvili E, Park J, et al. Prognostic utility of cell cycle progression score in men with prostate cancer after primary external beam radiation therapy. International Journal of Radiation Oncology, Biology, Physics. 2013;86(5):848–53.

47. Cooperberg MR, Simko JP, Cowan JE, Reid JE, Djalilvand A, Bhatnagar S, et al. Validation of a cell-cycle progression gene panel to improve risk stratification in a contemporary prostatectomy cohort. Journal of Clinical Oncology. 2013;31(11):1428–34.
48. Cuzick J, Berney DM, Fisher G, Mesher D, Moller H, Reid JE, et al. Prognostic value of a cell cycle progression signature for prostate cancer death in a conservatively managed needle biopsy cohort. British Journal of Cancer. 2012;106(6):1095–9.
49. Bauman G, Breau RH, Kamel-Reid S, Louie AV, Pautlere S. Ontario health technology assessment series: Prolaris cell cycle progression test for localized prostate cancer: A health technology assessment. 2017;17(6):1–75.
50. Bishoff JT, Freedland SJ, Gerber L, Tennstedt P, Reid J, Welbourn W, et al. Prognostic utility of the cell cycle progression score generated from biopsy in men treated with prostatectomy. J Urol. 2014;192(2):409–14.
51. Shahait M, Liu VYT, Vapiwala N, Lal P, Kim J, Trabulsi EJ, et al. Impact of Decipher on use of post-operative radiotherapy: Individual patient analysis of two prospective registries. BJUI Compass. 2021;2(4):267–74.
52. Carrion DM, Rivas JG, Alvarez-Maestro M, Martinez-Pineiro L. BIOMARKERS IN PROSTATE CANCER MANAGEMENT. IS THERE SOMETHING NEW? Archivos Espanoles De Urologia. 2019;72(2):105–15.
53. Fine ND, LaPolla F, Epstein M, Loeb S, Dani H. Genomic Classifiers for Treatment Selection in Newly Diagnosed Prostate Cancer. BJU International. 2019;04:04.
54. Health Quality Ontario. Prolaris Cell Cycle Progression Test for Localized Prostate Cancer: A Health Technology Assessment. Ontario Health Technology Assessment Series. 2017;17(6):1–75.
55. Jairath NK, Dal Pra A, Vince R, Jr., Dess RT, Jackson WC, Tosoian JJ, et al. A Systematic Review of the Evidence for the Decipher Genomic Classifier in Prostate Cancer. European Urology. 2021;79(3):374–83.
56. Lamy PJ, Allory Y, Gauchez AS, Asselain B, Beuzeboc P, de Cremoux P, et al. Prognostic Biomarkers Used for Localised Prostate Cancer Management: A Systematic Review. European Urology Focus. 2018;4(6):790–803.
57. Spratt DE, Zumsteg ZS, Feng FY, Tomlins SA. Translational and clinical implications of the genetic landscape of prostate cancer. Nature Reviews Clinical Oncology. 2016;13(10):597–610.
58. Bostrom PJ, Bjartell AS, Catto JW, Eggener SE, Lilja H, Loeb S, et al. Genomic Predictors of Outcome in Prostate Cancer. European Urology. 2015;68(6):1033–44.
59. Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, et al. 2020. SEER Cancer Statistics Review, 1975–2017. Accessed at National Cancer Institute at https://seer.cancer.gov/csr/1975_2017 on March 22 2022.
60. Evangelista L, Zattoni F, Cassarino G, Artioli P, Cecchin D, dal Moro F, et al. PET/MRI in prostate cancer: a systematic review and meta-analysis. European Journal of Nuclear Medicine and Molecular Imaging. 2021;48(3):859–73.

61. Krauss DJ, Karrison T, Martinez AA, Morton G, Yan D, Bruner DW, et al. Dose-Escalated Radiotherapy Alone or in Combination With Short-Term Androgen Deprivation for Intermediate-Risk Prostate Cancer: Results of a Phase III Multi-Institutional Trial. Journal of Clinical Oncology. 2023;41(17):3203–16.
62. Ilic D, Evans SM, Allan CA, Jung JH, Murphy D, Frydenberg M. Laparoscopic and robotic-assisted versus open radical prostatectomy for the treatment of localised prostate cancer. Cochrane Database of Systematic Reviews. 2017(9).
63. Jackson WC, Tang M, Schipper MJ, Sandler HM, Zumsteg ZS, Efstathiou JA, et al. Biochemical Failure Is Not a Surrogate End Point for Overall Survival in Recurrent Prostate Cancer: Analysis of NRG Oncology/RTOG 9601. Journal of Clinical Oncology. 2022;40(27):3172–9.
64. The Leeds Teaching Hospitals NHS Trust 2020. Prolaris Enhanced Risk Stratification - an ecONomic and clinicAL Evaluation (PERSONAL). Accessed at https://clinicaltrials.gov/ct2/show/study/NCT03851211. on January 16 2023.
65. Myriad Genetic Laboratories Inc. 2018. Clinical Outcomes in Men With Prostate Cancer Who Selected Active Surveillance Using Prolaris® Testing (URO-009Low). Accessed at https://clinicaltrials.gov/ct2/show/results/NCT03511235 on January 16 2023.
66. Shore ND, Boczko J, Kella N, Moran BJ, Crawford ED, Hamilton SA, et al. Impact of CCP test on personalizing treatment decisions: Results from a prospective registry of newly diagnosed prostate cancer patients. Journal of Clinical Oncology. 2015;33(7_suppl):63-.
67. Myriad Genetic Laboratories Inc. 2017. Registry to Measure the Impact of Adding Genomic Testing. Accessed at https://clinicaltrials.gov/study/NCT02454595?tab=results on January 16 2023.
68. Ong CW, Maxwell P, Alvi MA, McQuaid S, Waugh D, Mills I, et al. A gene signature associated with PTEN activation defines good prognosis intermediate risk prostate cancer cases. J Pathol Clin Res. 2018;4(2):103–13.
69. Yoon J, Kim M, Posadas EM, Freedland SJ, Liu Y, Davicioni E, et al. A comparative study of PCS and PAM50 prostate cancer classification schemes. Prostate Cancer and Prostatic Diseases. 2021;24(3):733–42.
70. Zhao SG, Chang SL, Spratt DE, Erho N, Yu M, Ashab HA, et al. Development and validation of a 24-gene predictor of response to postoperative radiotherapy in prostate cancer: a matched, retrospective analysis. Lancet Oncology. 2016;17(11):1612–20.

Figures

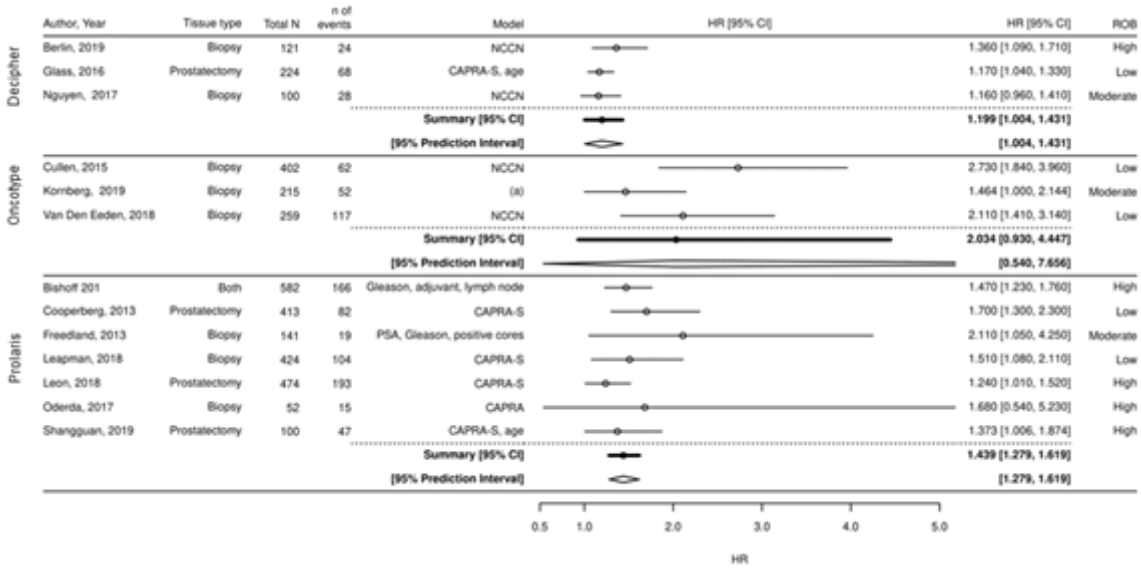

Figure 1

Hazard Ratio Forest Plot for Biochemical Recurrence by Test Type (Decipher, Oncotype, Prolaris)

[a] Model includes CAPRA, PSA, age, tissue source (confirmatory vs diagnostic biopsy), clinical institution (UCSF vs other), genomic prostate score testing (clinical care vs research).

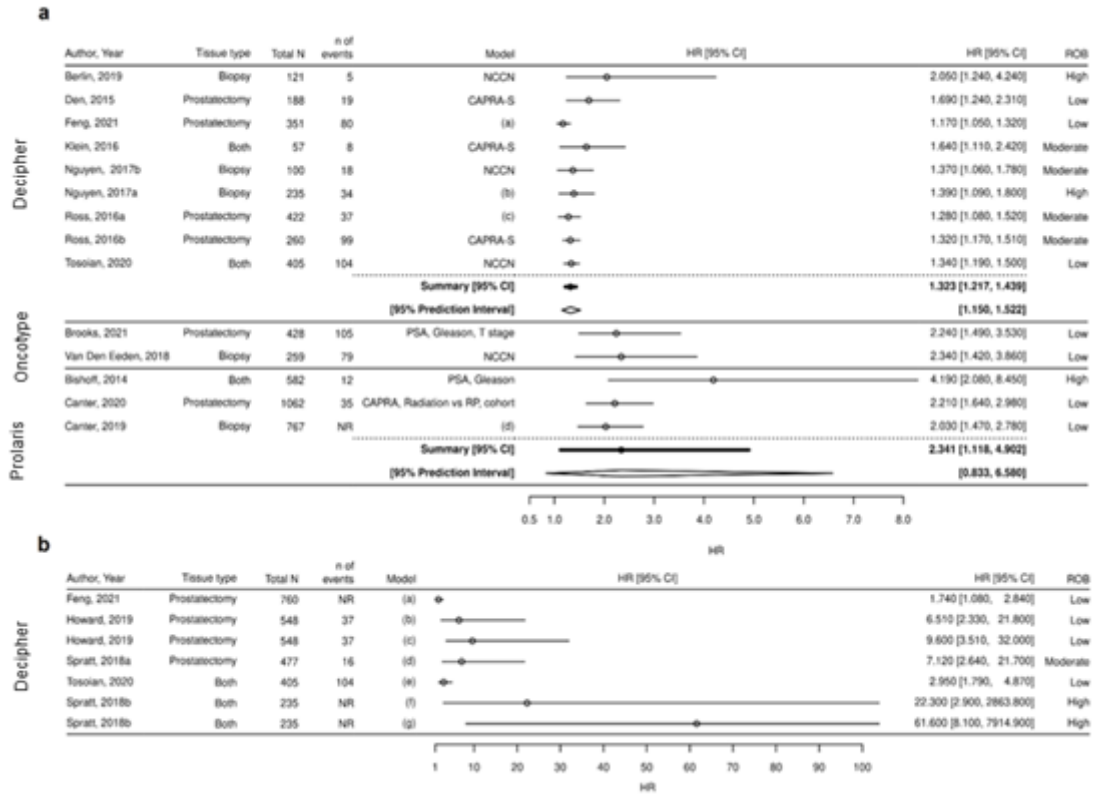

Figure 2

a. Hazard Ratio Forest Plot for Metastasis by Test Type (Decipher, Oncotype, Prolaris) b. Hazard Ratio for Categorical Studies Reporting Metastasis by Test Type (Decipher)

Plot a.

[a] Model includes age (≥ 65 vs <65), race (AA vs Non-AA), Gleason score (8-10 vs ≤ 7), T stage

(pT3 vs pT2), PSA, positive surgical margins, PSA nadir status (non-nadir vs nadir <0.5), ADT vs placebo.

[b] Model includes age, log2 (PSA), grade group, clinical stage, first-line treatment RP, first-line treatment RT ADT.

[c] Model includes CAPRA-S, treatment (adjuvant radiation vs minimal residual disease salvage radiation, salvage radiation, no radiation).

[d] CAPRA, ancestry (AA vs non-AA), primary treatment.

Plot b.

[a] Treatment, age, Black men vs non Black men, Gleason, T score, PSA, margin status, nadir, Decipher (high vs low).

[b] CAPRA-S, age, Black men vs non Black men, Decipher (intermediate vs low).

[c] CAPRA-S, age Black men vs non Black men, Decipher (high vs low risk).

[d] CAPRA-S, PSA, Decipher (high vs low/intermediate).

[e] Age, PSA, Grade Group, T-stage, Decipher (high vs low).

[f] Clinical-genomic risk grouping NCCN + Decipher (intermediate vs low).

[g] Clinical-genomic risk grouping NCCN + Decipher (high vs low).

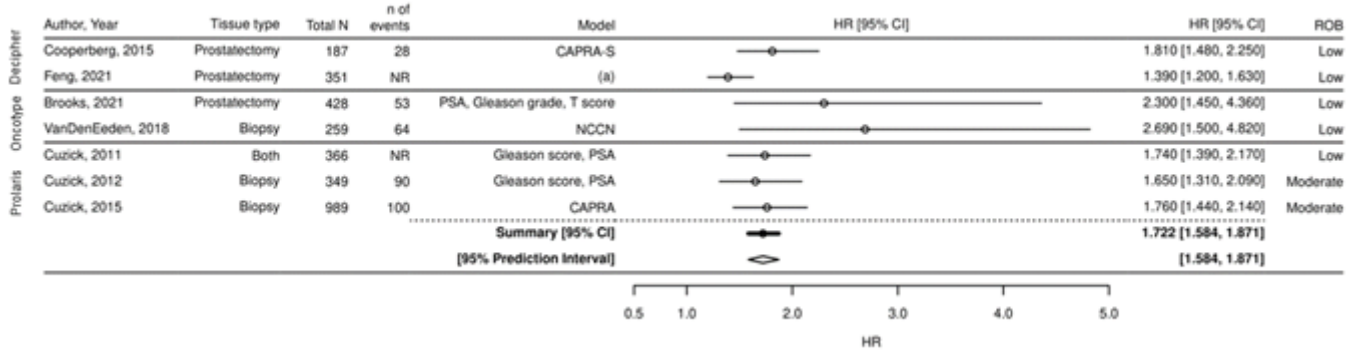

Figure 3

Hazard Ratio Forest Plot for Prostate Cancer–Specific Mortality by Test Type (Decipher, Oncotype, Prolaris)

[a] Model includes age (≥ 65 vs <65), Black men vs non Black men, Gleason score (8-10 vs ≤ 7), T stage (pT3 vs pT2), PSA at trial entry, positive surgical margins, PSA nadir status (non-nadir vs nadir <0.5), ADT vs placebo.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Genomicsandprostatecancerappendixfigures6.28.23AMG.docx
- Genomicsandprostatecancerappendixtables6.27.23.docx