Evidence table 1: Clinical validity – Decipher using biopsy specimen

Authors, Aim, Country	Methods	Patient's characteristics & Findings	RoB
Authors: (Berlin et al., 2019) Aim: test the utility of the GC to better identify patients with IR-PCa who are sufficiently treated by RT alone. Country:	Design: Retrospective study N=121 Inclusion criteria: Men diagnosed with NCCN-defined IR-PCa treated with curative-intent DE-IGRT without neoadjuvant, concomitant, or adjuvant ADT. Exclusion criteria: Index test: Decipher (GC scores) Comparator/reference standard: NCCN risk classification Study period: 2005-2011 Primary outcome: biochemical failure (PSA nadir + 2 ng/mL), Secondary outcome: metastasis occurrence Berlin et al., 2019 designed a retrospective study of 121 patients with Intermediate risk (IR) PCa treated with dose escalated RT without ADT (hormone Tx). The authors reported that GC was a significant predictor of biochemical failure (HR 1.33 (1.08 – 1.66), P=0.009) and metastasis (HR 2.05 (1.24 – 4.23), P=0.003). GC had a fair/good performance as its AUC for predicting biochemical failure and early onset metastasis were 0.78 and 0.86 respectively. The combination of GC with NCCN criteria had the best performance (AUC 0.85, 0.89 respectively). NCCN criteria were not predictor of biochemical or metastasis relapse. None of the conventional clinical indices (age, PSA, GS, clinical T category) were predictor of biochemical failure. The risk of bias of the study is high.	**Patient's characteristics:** Patients with Intermediate risk (IR) PCa treated with dose escalated RT without ADT (hormone Tx) N=121; 33 (27.3%) NCCN-favorable and 87 (71.9%) NCCN-unfavorable IR-PCa Median follow-up: 7.5 years (range, 6.5-8.7 years) Age: 72.4 y (68.4-75.0) Race: PSA: Prediagnostic PSA (median [IQR]), ng/mL: 7.8 (5.7-11.2) GS (ISUP): 2 (3 + 4): 75 (62.0%) Clinical T stage: cT1c/T2a 95 (78.5%) Biopsy grade groups: NCCN risk groups: Unfavorable, 87 (71.9%) **Findings:** Overall, GC classified 73% (n=88) as low risk (GC score <0.45), 15% (n=18) as intermediate (GC 0.45-0.6), and 12% (n=15) as high risk (GC >0.6). In the NCCN unfavorable subgroup, GC classified 60 (69.0%), 15 (17.2%), and 12 (13.8%) cases into low, intermediate, and high risk, respectively. In the NCCN favorable subgroup, GC classified 3 of 33 (9.1%) as high risk. The combination of NCCN and GC classification based on the clinicogenomic risk group identified a similar number of high-risk cases compared to using GC alone (9.9% (n=12)). **NCCN classification** / **GC** / P values Risk of biochemical failure: Not a predictor of biochemical relapse P =0.235 / GC is a predictor of biochemical failure HR 1.33 [1.08-1.66], P=0.009 Risk of metastasis: Not a predictor of metastasis relapse P=0.885 / GC is a predictor of metastasis 2.05 [1.24-4.23], P=0.003 AUC for prediction of biochemical failure: 0.56 / 0.78 0.85 for combination GC+NCCN AUC for prediction for early onset metastatsis: 0.54 / 0.86 0.89 for combination GC+NCCN AUC, Area Under the Curve. None of the conventional clinical indices (age, PSA, GS, clinical T category) were predictor of biochemical failure.	Conclusion: The findings demonstrate the utility of GC in combination with NCCN criteria for selecting IR-PCa to receive ADT and RT. GC reclassified an important number of patients as low risk despite having unfavorable clinicopathologic risk factors. The findings highlight the importance of incorporating GC in localized PCa prognostic system, which permits the identification of IR-PCa who can be treated with RT without ADT. RoB: Patient selection: high risk as the practice embraced the combination of RT and short-term ADT. Index test: low risk Reference standard: Flow of patients: low risk Concerns about applicability: low Others: retrospective design, small sample size Overall RoB: High

<table>
<tr><td></td><td></td><td></td><td></td></tr>
<tr>
<td>Authors: (Kim et al., 2019)

Aim: to assesses a role for Decipher in predicting adverse pathology (AP).

Country: USA</td>
<td>Design: Retrospective study

N=266

Inclusion criteria: NCCN-very-low/low or favorable-intermediate risk PCa patients who underwent diagnostic prostate biopsy between 2000 and 2014 and were treated with RP. Patients with complete tumor pathology from biopsy and prostatectomy and Decipher genomic expression
profiles generated from diagnostic biopsy specimens were selected for analysis.

Exclusion criteria: NCCN very-low-/lowor favorable intermediate-risk PC pts who underwent diagnostic prostate biopsy and were tx'd w/ RP

Index test: Decipher scores

Comparator/reference standard: Cancer of the Prostate Risk Assessment (CAPRA) scores

Study period: 2000 -2014

Primary outcome: association between Decipher and AP.</td>
<td>Patient's characteristics:
NCCN-very-low/low (65%) or favorable-intermediate risk (35%) PCa patients who underwent diagnostic prostate biopsy between 2000 and 2014 and were treated with RP. They were candidates for active surveillance (AS).
Median Age: 62 y
Race:
PSA: 5.4 ng/mL (interquartile range [IQR] 4.16ng/mL–7.19 ng/mL).
GS 4 and higher: 27 (10.2%)
Clinical stage: 85% diagnosed with cT1

Biopsy grade groups: 76% were in biopsy grade group 1

NCCN risk groups: 172 (64.7)

CAPRA risk groups: 186 (69.9%) and 76 (28.6%) were classified as CAPRA low & intermediate respectively.

71 (26.7%) were pT3a and 5 (1.9%) were pT3b.

Median Decipher 0.28 (IQR 0.17–0.39) and was significantly higher among men with AP (0.34 IQR 0.25–0.47 vs 0.27 IQR 0.15–0.37, p-value < 0.001

Rate of AP: 11% (19/172) and 14% (13/94) for the NCCN-very-low/low and favorable-intermediate patients, respectively.

Findings:
<table>
<tr><td></td><td>Decipher</td><td>CAPRA</td></tr>
<tr><td>Prediction of AP</td><td>1.29 (95% CI 1.03–1.61, p-value 0.025)
Decipher was a predictor of AP</td><td>was not a predictor of AP.</td></tr>
<tr><td>AUC</td><td></td><td>0.57
(95% CI 0.47–0.68).
0.65 with combination of CAPRA & Decipher</td></tr>
</table>
AUC increased when adding Decipher to NCCN (data not shown)

Sensitivities & specificities of different Decipher thresholds were assessed. As the threshold decreased, sensitivities increased, and specificities decreased.
Thresholds Sens Spe
0.45 28% (16–45%) 84% (78–88%)
0.40 34% (20–52%) 79% (73–83%)
0.20 88% (72–95%) 36% (30–42%)</td>
<td>Conclusion: Decipher was a significant predictor of AP when used alone, or with CAPRA, or NCCN. It can be applied to prostate biopsies from NCCN very-low/low and favorable-intermediate risk patients to predict AP found in prostatectomy pathology that would contribute to decision making.

Patient selection: possibility of selection bias
Index test: Low risk
Reference standard: Low risk
Flow of patients: Low
Concerns about applicability:
Others: study design; No long-term follow-up to consider survival outcomes, small sample size and low number of events did not allow Decipher to be evaluated in individual NCCN risk.

Overall RoB: High</td>
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<td>For Decipher thresholds of 0.45 and 0.2, NPV was 91% (95% CI 87-94%) and 96% (95% CI 90-99%).

Using a threshold of 0.2, Decipher was a significant predictor of AP when adjusting for CAPRA (p-value 0.016). Patients with Decipher >0.2 were more likely to have AP (OR 3.17, 95% CI 1.22–10.26) than patients with Decipher ≤ 0.2.</td>
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<tr>
<td>Authors: (Nguyen, Haddad, et al., 2017)

Aim: To assess the ability of biopsy Decipher to predict metastasis and Prostate cancer-specific mortality (PCSM) in primarily intermediate- to high-risk patients treated with RP or radiation therapy (RT).

Country: USA</td>
<td>Design: Retrospective study

N=235 (n=105 RP, n=130 RT)

Inclusion criteria: Patients treated with either first-line RP or first-line RT ± ADT from 1987 to 2014 with available genomic expression profiles. Genetic profiles derived from biopsy specimens. Patients with NCCN intermediate- and high-risk disease were included. RP cohort had adverse pathology at surgery (preoperative PSA > 20 ng/ml, stage pT3 or margin positive, or RP Grade Group ≥ 4).

Exclusion criteria:

Index test: Decipher

Comparator/reference standard: NCCN, Cancer of the Prostate Risk Assessment (CAPRA)

Follow-up: 6 years

Primary outcomes: Metastasis
Secondary outcome: PCSM</td>
<td>Patient's characteristics:
Median Age: 64 y (at Tx)
Race:
Median PSA: 7.0 ng/ml
GS:
Clinical stage: 53% had clinical stage T2a or higher
Biopsy grade groups: 53% of patients had biopsy Grade Groups 2 and 3
NCCN risk groups: 54% and 32% were intermediate and high-risk patients based on NCCN risk group respectively
CAPRA risk groups: 48% and 26% were intermediate and high-risk patients based on NCCN risk group respectively.
Median CAPRA score: 4
Median Decipher score: 0.39

Findings:
34 patients developed metastases and 11 died of prostate cancer.
<table>
<tr><th></th><th>Decipher</th><th>CAPRA</th><th>NCCN</th></tr>
<tr><td>Prediction of metastasis</td><td>HR 1.37 (1.06–1.78, p = 0.018)

Similar HR was reported when controlled for CAPRA, NCCN (data not shown).

HR 1.39 (1.09–1.8) p=0.009 when adjusted for Tx & clinical data</td><td></td><td></td></tr>
<tr><td>Prediction of metastasis 5-yr post-biopsy – measured by C-index (C-index assessed discriminatory performance)</td><td>0.74 (95% CI: 0.63–0.83) Significant</td><td>0.60 (0.50–0.69) Not significant

CAPRA + Decipher: 0.71 (0.60 – 0.82) Addition of Decipher to CAPRA significantly improved C-index</td><td>0.66 (95% CI: 0.53–0.77) Significant

NCCN + Decipher: 0.74 (95% CI: 0.66–0.82) Addition of Decipher improved C-index</td></tr>
</table></td>
<td>Decipher can predict metastasis and prostate cancer-specific mortality in biopsy
specimens of intermediate- and high-risk patients treated with RT or RP.

Patient selection: Low
Index test: unclear (lack of information on whether index test was interpreted without knowledge of comparator/standard reference)
Reference standard: unclear (lack of information on whether comparator/reference standard was interpreted without knowledge of index test)
Flow of patients: Low
Concerns about applicability for patient selection, index test, reference standard: Low
Other: retrospective study, small sample size, short follow-up (larger sample size & longer follow-up would have led to more mortality events), since most patients were NCCN intermediate and high-risk, no conclusion could be drawn regarding low-risk patients.

Overall quality is low.</td>
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		<table><tr><td>Superiority based on decision curve analysis</td><td>Decipher superior to CAPRA</td><td></td><td></td></tr><tr><td>Stratification of metastasis risk</td><td>Decipher Risk level: metastasis rate Low: 4% Intermediate: 8% High risk: 21 %</td><td>Similar findings to those of NCCN.</td><td>low, intermediate, and high risk had 0%, 6.4%, and 14% metastasis rate</td></tr><tr><td>Prediction of PCSM</td><td>only Decipher significantly stratified PCSM risk (p =0.008) HR1.57 (1.03–2.48) p = 0.037 Patients with low-, intermediate- and high-risk Decipher had a 0%, 0%, and 9.4% incidence of PCSM by 5-yr post-treatment</td><td>Not significant</td><td>Not significant</td></tr><tr><td></td><td></td><td></td><td></td></tr></table> Sensitivity analysis (including only intermediate to high-risk disease, n=203) showed that decipher maintained its prognostic value for distant metastasis after controlling for CAPRA (HR of 1.41, 95% CI: 1.12–1.80).	
Authors: (Nguyen, Martin, et al., 2017) Aim: To assess the ability of GC to predict metastasis after radiation and 6 months of androgen deprivation therapy (ADT). Country:	Design: Retrospective study N=100 Inclusion criteria: patients who received radiation and ADT from 2001 – 2013 and who had NCCN intermediate or high-risk prostate cancer and had archived tissue available. Exclusion criteria: Inadequate tumor tissue for RNA extraction, patients who did not pass prespecified microarray quality control thresholds. Index test: Decipher GC scores Comparator/reference standard: CAPRA, NCCN	**Patient's characteristics:** Patients had NCCN intermediate and high risk prostate cancer who received radiation and ADT. Age: 67 years (range, 45–87) Race: PSA: 7.3 ng ml− 1 (IQR 4.7–-14.9 ngml− 1) GS:36%, 23%, and 19% had GS 7 (4+3), 7 (3+4), and ≥9 respectively. Clinical stage: 64% (64) ⩽T2a Biopsy grade groups: NCCN risk groups: 55% (55) were classified as intermediate risk while 45% (45) were high-risk CAPRA risk groups:	Conclusion: GC can predict for distant metastases after definitive radiation and ADT in men with intermediate and high risk prostate cancer. GC outperformed NCCN & CAPRA and predict with accuracy the 5-year risk of distant metastases. However, GC is not associated with biochemical failure. Patient selection: Index test: unclear Reference standard: unclear Flow of patients: Low Concerns about applicability: Low

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<td>Follow-up: 5.1 years
(interquartile range: 3.4-6.3)

Primary outcome: distant metastasis following radiation tx.
Secondary outcome: biochemical failure (nadir plus 2 definition) and castrate resistance (defined as any rise in PSA despite being on salvage ADT for biochemical failure).</td>
<td>18 patients developed metastasis during study follow-up; 28 patients had biochemical failure; 12 developed castrate resistant disease.

Findings:
Median GC score was 0.39 (IQR: 0.22–0.61).
The median CAPRA score was 5 (IQR: 4–6)

<table>
<tr><th></th><th>Decipher</th><th>CAPRA</th><th>NCCN</th></tr>
<tr><td>Prediction of metastasis</td><td>HR 1.40 (1.10–1.84); P = 0.006</td><td>HR 1.15 p=0.271
Not significant</td><td>HR 2.00 (0.78-5.35);
P = 0.147 Not significant</td></tr>
<tr><td></td><td colspan="3">Only Decipher was a significant predictor of metastasis
Decipher remained a significant predictor of metastasis in models including CAPRA or NCCN (HR not shown).</td></tr>
<tr><td>Biochemical failure</td><td colspan="3">None of tests are predictors of biochemical failure. CAPRA in univariate analysis was predictor of biochemical failure HR: 1.23; 95% CI: 1.01-1.49; P = 0.042;</td></tr>
<tr><td>castrate resistant disease</td><td colspan="3">After adjusting for NCCN
HR for GC 1.43 (1.01-2.09); P =0.044

After controlling for CAPRA
HR for GC 1.48 (1.00–2.45); P =0.049</td></tr>
<tr><td>Discrimination performance – Survival C-index at 5 years post radiation. [C-index is AUC]</td><td>0.76 (95% CI: 0.57–0.89)

This is significant
C-index is good</td><td>0.45 (95% CI: 0.27–0.64)

Not significant</td><td>0.63 for NCCN (95% CI: 0.40–0.78)
Not significant</td></tr>
<tr><td>Survival c-index of GC for predicting metastasis at 10 years following RT</td><td>0.78 (95% CI: 0.60–0.87)</td><td></td><td></td></tr>
<tr><td>Decision curve analysis</td><td colspan="3">Showed that the net benefit of using GC for treatment decision was generally higher than basing clinical decisions on either the CAPRA risk model or naively choosing to either treat all patients or to treat none.</td></tr>
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</td>
<td>Other: small sample size, short follow-up, retrospective design; Conflict of interest was reported.

Overall, the quality of the study is low.</td>
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<tr>
<td colspan="4">Authors: (Klein et al., 2016):This study was excluded because less than 100 patients had Decipher test.
(Press et al., 2022) was excluded because distant metastasis, biochemical failure, or mortality was not evaluated</td>
</tr>
<tr>
<td>Authors:

Aim:

Country:</td>
<td>Design:

N=

Inclusion criteria:

Exclusion criteria:</td>
<td>Patient’s characteristics:
Age:
Race:
PSA:
GS:
Clinical stage:

Biopsy grade groups:</td>
<td>Patient selection:
Index test:
Reference standard:
Flow of patients:
Concerns about applicability:
Others:</td>
</tr>
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	Index test: Comparator/reference standard: Follow-up: Primary outcomes:	NCCN risk groups: CAPRA risk groups: **Findings:**	

Evidence table 2: Decipher test using RP specimens

<table>
<tr><th>Authors, Aim, Country</th><th>Methods</th><th>Patient's characteristics & Findings</th><th>RoB</th></tr>
<tr><td colspan="4">Clinical Validity</td></tr>
<tr><td>Authors: (Herlemann et al., 2020)

Aim: to validate Decipher to predict adverse pathology (AP) in patients who underwent radical prostatectomy (RP) with NCCN favorable-intermediate risk (F-IR) prostate cancer (PCa), and to improve selection of F-IR candidates for active surveillance (AS).

Country: USA</td><td>Design: retrospective

N=647 n=220 for F-IR patients

Inclusion criteria: Patients diagnosed with NCCN very low/low risk (VL/LR) or favorable Intermediate Risk (F-IR) prostate cancer who underwent RP with complete postoperative clinicopathological information and Decipher genomic risk scores.

Exclusion criteria:

Index test: Decipher

Comparator/reference standard: CAPRA

Study period:

Primary outcome: Prognostic ability of Decipher to predict Adverse Pathology (AP) (defined as grade group 3−5, pT3b or higher, or lymph node invasion) at RP within the NCCN F-IR group while considering CAPRA.</td><td>Patient's characteristics:
Patients diagnosed with NCCN very low/low risk (VL/LR) or favorable Intermediate Risk (F-IR) prostate cancer who underwent RP with complete postoperative clinicopathological information and Decipher genomic risk scores.

The following characteristics were reported for NCCN F-IR cohort:
Median Age: 61 y (56 - 66)
Race: majority were White 63%
PSA: 5.9 ng/mL (IQR 4.6–9.3)
GS:
Clinical stage: majority (67%) had cT1

Biopsy grade groups: majority (62%) had GG2

NCCN risk groups: 100% were F-IR

CAPRA risk groups: CAPRA classified 53% as low risk (0-2) and 47% as intermediate risk (3-5). Majority of the F-IR patients were CAPRA 2 or 3

Decipher classified 79% as low risk, 13% as intermediate risk, and 8% as high-risk

median time from biopsy to RP was 3 months

After RP, 74% had pathological stage pT2 and 18% had positive margins

Overall 15% had AP at RP, 15% GG 3−5 only and 33% AP-II.

BCR at 3 years was 4% with a median follow-up of 2.8 years

Findings: for NCCN F-IR cohort
<table>
<tr><th></th><th>Decipher</th><th>CAPRA</th></tr>
<tr><td>Prediction of AP</td><td>OR=1.34 (1.1−1.6) P= 0.002. This remained significant after controlling for CAPRA.</td><td>OR 1.6 (1.0−2.7) not significant</td></tr>
</table></td><td>Conclusion:
The study demonstrated that Decipher is an independent predictor of AP among patients with NCCN F-IR with higher likelihood of AP at the time of RP. CAPRA is not a significant predictor of AP in this group.

Among these patients, only Decipher high risk had higher odd of predicting AP compared to low risk.

NCCN F-IR had increased odds (1.7 OR) of adverse pathology as compared to NCCN VL/LR tumors.

A small subset (3%) of F-IR patients with Decipher high-risk results had increased risk of AP compared to VL/LR tumors.

RoB:
Patient selection: Low
Index test: unclear (lack of information to whether the results of reference standard was known to those who interpreted the Decipher test and vice versa)
Reference standard: unclear
Flow of patients: Low risk
Concerns about applicability:
Other: retrospective design, COI.

Overall, RoB is high.</td></tr>
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<table>
<tr><td>Prediction of AP</td><td>Compared to low risk, Decipher high-risk (3% only), but not intermediate-risk, predicted AP with OR of 4.6 (95% CI 1.6−12.9).</td><td></td></tr>
<tr><td>AUC</td><td></td><td>0.60 (95% CI 0.51–0.70)

Adding Decipher increased the AUC to 0.65 (0.57–0.71)</td></tr>
</table>

Analysis of NCCN F-IR (n=220) vs NCCN VL/Low risk (n=427)
<table>
<tr><td></td><td>NCCN F-IR cohort</td><td>NCCN VL/Low risk</td></tr>
<tr><td>Prediction of AP</td><td colspan="2">OR 1.7, 95% CI 1.0−2.8, p < 0.05
NCCN F-IR had increased
Odds of AP as compared to NCCN VL/LR tumors.</td></tr>
<tr><td>AP rate at RP</td><td></td><td>9%</td></tr>
<tr><td>Odd of AP</td><td colspan="2">NCCN F-IR with a Decipher high-risk score had a significantly higher
odds for AP of 6.8 (p < 0.001) compared to VL/LR tumors.</td></tr>
<tr><td></td><td></td><td></td></tr>
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<td>Authors: (Tosoian et al., 2020)

Aim: To assess the performance of Decipher within NCCN high-risk disease.

Country:</td>
<td>Design: Retrospective study

N= 405 patients

Inclusion criteria: Patients with high-risk prostate cancer who underwent primary treatment with radical prostatectomy (RP) or radiation therapy (RT) with androgen-deprivation therapy (ADT).

Exclusion criteria:</td>
<td>Patient’s characteristics:
Patients with high-risk prostate cancer who underwent RP or RT with ADT.

Age:
Race:
PSA:
GS:
Clinical stage:

Biopsy grade groups:</td>
<td>Decipher is an independent predictor of metastasis in patients with high-risk prostate cancer who underwent RP or RT. Clinico-pathologic variables have a poor discrimination to risk stratify metastatic disease. The addition of Decipher to these variables increase their performance.</td>
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	Index test: Decipher test Comparator/reference standard: clinico-pathologic variables, CAPRA, Follow-up: 82 months Outcomes: Metastasis, performance AUC	NCCN risk groups: CAPRA risk groups: **Findings:** 26% (104/405) developed metastasis Association with metastasis: GC score was significantly associated with metastasis (HR: 1.33 (1.19-1.48, p < 0.001)) GC high-risk (vs low risk) was significantly associated with metastasis, HR: 2.95 (1.79-4.87, p < 0.001)). AUC: Addition of GC to NCCN risk group increased AUC from 0.46 to 0.67. Addition of GC to CAPRA increased AUC from 0.59 to 0.71.	Study was based on Abstract. All the patients' characteristics were not known but patients had high-risk prostate cancer. The RoB was based on study design only. Main limitation: retrospective study Overall RoB: High
(Howard et al., 2020) Aim: To evaluate GC and compare its performance to CAPRA-S in African Americans (AA) and non-AA.	Design: N=548 Inclusion criteria: Patients with high-risk disease with either pT3a, positive margins, seminal vesicle invasion, or received post-RP radiotherapy. Follow-up (median): 9 years	**Patients' characteristics:** Patients with high-risk disease and was selected to have either pT3a, positive margins, seminal vesicle invasion, or received post-RP radiotherapy. **Findings**: AA number: 55% (301/548) Metastasis: 37/548 Mortality: 20/548 Association btw Decipher & metastasis: GC was an independent predictor of metastasis with p<0.001 (in AA as well as non-AA) Performance: measured by C-index (Decipher vs CAPRA-s) C-index (for 5-year metastasis): 0.78 vs. 0.72 C-index (10-year PCSM): 0.85 vs. 0.81	Decipher is a significant predictor of metastasis and mortality among African Americans & non-AA with high-risk who underwent RP. Rob: This is an abstract. Determination of Rob was challenging in the absence of the methodology.
Authors:(Feng et al., 2021)	Design: Validation study of GC in RCT RP specimens were derived from patients on placebo-controlled RCT of salvage radiotherapy (sRT) +/- 2 years of bicalutamide. These	**Patient's characteristics:** RP specimens were derived from patients on placebo-controlled RCT of salvage radiotherapy (sRT) +/- 2 years of bicalutamide. In the RCT, patients were required to have recurrent disease after RP with a PSA of 0.2 to 4.0 ng/mL, pathologic T3 disease	Conclusion: GC is a significant predictor of distant metastasis, prostate cancer mortality, and overall survival independent of

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<td>Aim: validate the GC within the context of a randomized phase 3 trial.

Country:</td>
<td>specimens were centrally reviewed and underwent RNA extraction. GC scores were generated.

N=352/522 passed QC

Inclusion criteria in the RCT where specimens were obtained: patients were required to have recurrent disease after RP with a PSA of 0.2 to 4.0 ng/mL, pathologic T3 disease (tumor spread beyond the prostate) or T2 disease (tumor contained within the prostate) with a positive surgical margin and no evidence of nodal or metastatic disease.

Exclusion criteria:

Index test: GC

Comparator/reference standard: standard clinicopathologic variables

Follow-up: 13 y

Primary outcome: Prognostic ability of the GC to independently predict the cumulative incidence of distant metastasis (DM).
Secondary outcome: prostate cancer-specific mortality (PCSM) and overall survival (OS).
.</td>
<td>(tumor spread beyond the prostate) or T2 disease (tumor contained within the prostate) with a positive surgical margin and no evidence of nodal or metastatic disease.
Age: 64.5 y
Race:
PSA: most had PSA <0.7 or PSA 0.2 -1.5 ng/ml
GS: majority had GS 7 or GS 2-6
T stage: most had T3

148 of 352 GC low (42%), 132 of 352 GC intermediate (38%), and 72 of 352 GC high risk (20%)

Findings:

<table>
<tr><th></th><th>GC</th></tr>
<tr><td>Ability to predict distant metastasis (DM)</td><td>HR 1.19 [95%CI 1.06-1.35], p=0.003</td></tr>
<tr><td>Prostate cancer specific mortality (PCSM)</td><td>HR 1.37 [95%CI 1.18-1.61], p<0.001)</td></tr>
<tr><td>Overall survival (OS)</td><td>HR 1.16 [95%CI 1.06-1.28], p=0.002</td></tr>
</table>

There was not a statistically significant interaction between GC score and hormone treatment effect for DM, mortality, and OS. However, the estimated absolute benefits in DM, PCSM, and OS observed with hormone therapy were different by GC risk groups; the 12-year benefit from the addition of hormone therapy was approximately 3-fold greater in intermediate and high GC scores than in low GC scores (all patients, low vs intermediate and high: DM, 5.0% vs 15.7%; PCSM, 4.5% vs 11.8%; OS, 2.4% vs 8.9%).

The GC score was prognostic also across other end points, including second biochemical recurrence (treatment arm: HR, 1.24; 95% CI, 1.10-1.39; P < .001), distant progression-free survival (treatment arm: HR, 1.19; 95% CI, 1.08-1.31; P < .001), and metastasis-free survival (treatment arm: HR, 1.17; 95% CI, 1.04-1.33; P = .008).</td>
<td>standard clinicopathologic variables (age, race/ethnicity, Gleason score, T stage, margin status, entry prostate-specific antigen, and treatment arm).

Limitations:
RP tissue were older than 20 years resulting in 30% quality control failure rate. Sample size is limited.</td>
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<tr>
<td>Authors: (Karnes et al., 2018)

Aim: Validate the 22 gene Decipher genomic classifier (GC) to predict PCSM in men with adverse pathologic features after RP.

Country:</td>
<td>Design: Retrospective study

N=561 (n=112 with PCSM10)

Inclusion criteria: Patients with adverse pathologic features: pT3, pN1, positive margins, or Gleason score >7 who underwent RP

Exclusion criteria: patients with neoadjuvant therapy. patients alive with less than 10 yr of follow-up.

Index test: Decipher</td>
<td>Patient’s characteristics:
Patients with adverse pathologic features: pT3, pN1, positive margins, or Gleason score >7 who underwent RP
Age:
Race:
PSA:
GS:
Clinical stage:

Biopsy grade groups:
Median GC score: 0.39 (0.23 – 0.59)
Median CAPRA-S: 4 (3, 6)
Patients with PCSM10 had similar characteristics to patients without except for Gleason, RP stage, CAPRA-s, GC, and adjuvant ADT or RT.</td>
<td>Conclusion: Decipher GC may be an independent predictor of prostate cancer specific mortality within 10 years of radical prostatectomy in men with adverse pathology.</td>
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	Comparator/reference standard: CAPRA, Follow-up: 13 y (patients without PCSM10). Primary outcomes: Association of GC and PCSM within 10 years of RP (PCSM10) (controlled for CAPRA); GC performance evaluated by AUC	**Findings:** <u>Association of GC & PCSM</u> GC was associated with PCSM within 10 years of RP adjusting for CAPRA; OR 1.34 (1.20, 1.50), P<0.001 Compared to low & intermediate GC score, high GC score (>0.6) was associated with PCSM 10 [OR 3.91 (2.43–6.29)] after adjusting for CAPRA-S with AUC of 0.77; <u>Performance by AUC</u> AUC of GC adjusted for CAPRA: 0.76 (95% CI 0.71, 0.82). This represented 0.03 increase of AUC from adding GC. AUC of GC high score adjusted for CAPRA: 0.77 (0.77, 0.81) suggesting an increase of 0.04 from adding GC. **IN Patients with high risk (PSA > 20 or prostatectomy Gleason score > 8 or prostatectomy stage pT3b/N1 [n = 323, 98 PCSM10]** GC is still associated with PCSM10 after adjusting for CAPRA-S [OR 1.33 (1.17, 1.50) P<0.001 with AUC of 0.69 (0.62, 0.75)]. Compared to low & intermediate GC score, high GC score + CAPRA-s was associated with PCSM 10 [3.96 (2.35, 6.69), P<0.001 with AUC of 0.69 (0.63, 0.76)] **Patients with BCR within 2 yr:** high GC score was associated with PCSM 10 [OR 3.06 (1.62, 5.76) P<0.001, with AUC 0.72 (0.65, 0.79)] adjusted for CAPRA-s. **Patients with metastasis** High GC score + CAPRA-s was associated with PCSM 10 [OR 1.95 (1.12, 3.39), P=0.02, with AUC of 0.64 (0.56, 0.71)].	case – control was not avoided. In fact, there was a combination of case-control & cohort study. The cohorts combine case-control and cohort study; adjuvant tx was administered to high-risk patients causing confounding. Patients were from academic centers compromising extrapolation to the general population. Overall, RoB is high.
(Dalela et al., 2017) Aim: to develop and internally validate a risk-stratification tool incorporating the Decipher score, along with routinely available clinicopathologic features, to identify patients who would benefit the most from aRT.	Design: Retrospective study N=512 Inclusion criteria: Patients in the randomly selected subcohort of casecohort studies Achieved PSA nadir after surgery Complete clinical data Received either adjuvant or salvage radiation or no	**Patient's characteristics:** Patients with prostate cancer treated with radical prostatectomy. Patients had ≥ pT3a disease, positive surgical margins, and/or pathologic lymph node invasion. Median Age: 61 Race: PSA: GS: ≥4+3 in 48.4% of patients, and the majority (72.3%) harbored extraprostatic disease. Pathologic stage: most were pT3a, pT3b Surgical margins: most have Sx margins (67%) Clinical stage:	Conclusion: The addition of Decipher score to a risk stratification model may provide incremental prognostic value in identifying patients with adverse pathologic features at higher risk of clinical recurrence. RoB: High

	radiation treatment before clinical evidence of metastasis Patients with pT3 disease or PSMs (Prostate surgical margins) Exclusion criteria: Patients who received any neo-adjuvant prostate cancer treatment before surgery Index test: Decipher test Comparator: Median Follow-up in censored patients: 8.3 years Primary outcome: time to clinical recurrence (CR; as documented from prostatic fossa biopsy specimen, and/or radiographically on computed tomography scan, bone scan, and/or other imaging modalities).	Median GC score: 0.41 (range 0.00 to 0.96) GC risk category: most were low & intermediate risk Patients who received aRT harbored PSMs more frequently than those who did not receive aRT (initial observation group) **Findings:** 21.9% (112/512) of patients received aRT 62/512 patients (12.1%) had documented CR. Decipher high risk is a significant predictor of clinical recurrence (CR): HR 2.93 (1.58 to 5.55), p=0. 001 Nomogram developed with decipher and ART status stratification: HR, 1.25 [95% CI, 1.09 to 1.44]; P=0.002 Discrimination accuracy of the novel nomogram for predicting 5-year CR risk was: 85% vs 79% for the clinicopathologic model (CI of the two models overlapped)	This is due to retrospective design, COI.
(Ross, Den, et al., 2016) Aim: To evaluate the combination of clinico-pathological and genomic risk in the context of postoperative therapeutic choices.	Design: Retrospective study N=422 Inclusion criteria: Patients with PCa treated with radical prostatectomy (RP) who had adverse pathological features, and no lymph node metastasis. All patients reached an undetectable PSA following surgery. Patients received either no post-operative treatment before development of metastasis or were treated with either ART or SRT. Exclusion criteria: Patients who received SRT with a pre-radiation therapy (RT) PSA 410 ng ml − 1 Index test: Decipher Comparator: CAPRA-s Median F/u: 8 years in those who did not develop metastasis	**Patients' characteristics** Patients with PCa treated with radical prostatectomy (RP) who had adverse pathological features, and no lymph node metastasis. 37/422 developed metastasis Demographics & clinical characteristics were similar btw treatment groups except for Extra prostatic extension and positive surgical margins rates. The no RT group had the lowest positive surgical margin rate and highest rate of extra prostatic extension. CAPRA classified 6, 58 and 36% of men low (0–2), intermediate (3–5) and high risk (6-12). The cumulative incidence of metastasis at 10 years post RP was 11.3, 3.3 and 21.4%, respectively. Decipher score classified 57, 27 and 16% as low (<0.45), intermediate (0.45–0.60) and high risk (40.60). Cumulative incidence of metastasis at 10 years post RP was 6.8, 10.3 and 21.9%. CAPRA-S and Decipher scores were independent predictors of metastasis. Multivariable analysis of treatment groups adjusted by Decipher and CAPRA-S Decipher HR 1.28 (1.08–1.52), P=0.004 CAPRA-S HR 1.39 (1.18–1.62), P=0.001 ART Reference 1 MRD-SRT HR 2.30 (0.51–10.33), P= 0.28	Conclusion: Decipher is an independent predictor of 10-year risk of metastasis. It may be used to improve tx decision in post prostatectomy in patients with adverse pathological features. Rob: Retrospective design; ascertainment bias may have accounted for differences between groups; sample size & few observed events may have limited study power; there is COI.

<table>
<tr>
<td></td>
<td>Primary outcome: Incidence of clinical metastasis (regional or distant) documented radiographically on computed tomography or bone scan.</td>
<td>SRT HR 4.31 (1.20–15.47) 0.02
No RT HR 5.42 (1.59–18.44), P=0.007

10-year risk of metastasis: Increased with rising scores for both Decipher & CAPRA
<table>
<tr><th>Decipher Score</th><th>ART</th><th>MRD-SRT</th><th>SRT</th><th>No RT</th></tr>
<tr><td>Low (<0.45)</td><td>2% (0-5%)</td><td>4% (0-9%)</td><td>10% (2-16%)</td><td>10% (4-16%)</td></tr>
<tr><td>Intermediate (0.45-0.60)</td><td>4% (0-8%)</td><td>6% (0-13%)</td><td>14% (2-24%)</td><td>15% (3-25%)</td></tr>
<tr><td>High (>0.60)</td><td>11% (0-23%)</td><td>19% (0-35%)</td><td>38% (13-56%)</td><td>40% (16-57%)</td></tr>
<tr><th>Panel A - CAPRA-S Score</th><th>ART</th><th>MRD-SRT</th><th>SRT</th><th>No RT</th></tr>
<tr><td>Low and Intermediate (0-5)</td><td>1% (0-3%)</td><td>3% (0-7%)</td><td>6% (1-10%)</td><td>6% (2-10%)</td></tr>
<tr><td>High (6-12)</td><td>8% (0-17%)</td><td>20% (0-36%)</td><td>32% (13-47%)</td><td>34% (18-47%)</td></tr>
</table>
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<tr>
<td>(Ross, Johnson, et al., 2016)

Aim: To evaluate the Decipher genomic classifier in a natural history cohort of men at risk who received no additional treatment until the time of metastatic progression.</td>
<td>Design: retrospective case-cohort design

N=356; n(for Decipher)=260

Inclusion criteria: Cancer of the Prostate Risk Assessment postsurgical (CAPRA-S) score ≥3; (2) pathologic Gleason score ≥7; and (3) post-RP prostate-specific antigen nadir <0.2 ng/ml.

Exclusion criteria: Metastasis prior to RP; Patients who received neoadjuvant tx, radiation and/or hormonal tx before metastasis.

Index test: Decipher

Comparator: CAPRA-s, clinicopathological factors

Follow-up: 9 y

Primary outcome: regional or distant metastases.</td>
<td>Patients' characteristics:
Men who underwent RP, at intermediate or high risk and received no additional treatment until the time of metastasis.
Patients had CAPRA-S score ≥3, pathologic GS≥7, post-RP PSA nadir <0.2 ng/ml.

Age: 60
Preop PSA: 9.5 ng/ml
53% had GS 7
Pathological GS: 37% had GS 3+4; 32% had GS ≥9

Findings
99 patients had metastasis among those in whom Decipher was obtained (n=260).

There was a significant correlation btw Decipher and incidence of biochemical recurrence, metastasis, and prostate cancer specific mortality (p<0.001).
10-year after RP, low Decipher score corresponded to 12% metastasis & high decipher score corresponded to 47% metastasis. Intermediate Decipher score corresponded to 31% metastasis.

Decipher was independently prognostic of metastasis HR 1.26 (1.08-1.47); p<0.01.

Model 2: CAPRA-S 1.60 (1.46-1.76); P<0.01; Decipher: 1.32 (1.17-1.51); P<0.01

Decipher C-index (C-index is similar to AUC): 0.76
Decipher increased the c-index of Eggener and CAPRA-S risk models from 0.76 and 0.77 to 0.86 and 0.87, respectively, at 10 yr after RP.</td>
<td>Conclusion:
Decipher is an independent predictor of metastasis in a population that received no adjuvant or salvage therapy after prostatectomy until metastatic progression. Higher decipher scores correlated with high rate of metastasis. There was correlation between decipher and mortality.
Decipher may increase the performance of other clinicopathologic risk models.

Risk of bias:
Retrospective design, single-center, 27% (96/356) patients did not have tumor blocks available; COI.</td>
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<td>(Glass et al., 2016)

Aim: determine the value of Decipher to predict</td>
<td>Design: retrospective study

N=224</td>
<td>Patients' characteristics:
Patients had aggressive prostate cancer with at least 1 of several criteria such as preoperative prostate specific antigen 20 ng/ml or greater, pathological Gleason score 8 or greater, stage pT3 disease or positive surgical margins at prostatectomy.</td>
<td>Conclusion: Decipher improved the prediction of cancer recurrence beyond that of</td>
</tr>
</table>

prostate cancer outcomes among patients after prostatectomy in a community health care setting.	Inclusion criteria: Patients had aggressive prostate cancer with at least 1 of several criteria such as preoperative prostate specific antigen 20 ng/ml or greater, pathological Gleason score 8 or greater, stage pT3 disease or positive surgical margins at prostatectomy. Patients who received no neoadjuvant therapy, and no adjuvant postoperative radiation therapy, hormonal therapy or chemotherapy. Exclusion criteria: Tumors with spread to regional nodes Intervention: Decipher Comparators: CAPRA-S (Cancer of the Prostate Risk Assessment Post-Surgical) score Median Follow-up of censored patients: 9 y (6-12) Primary outcome: clinical recurrence or metastasis after surgery evaluated using a time dependent c-index. Secondary outcomes: biochemical recurrence and salvage treatment failure; performance of Decipher in comparison to CAPRA-s; Contributions of Decipher, CAPRA-S and their combination for the prediction of recurrence and treatment failure.	Median age (IQR): 57 (46-64) Median ng/ml preop PSA (IQR): 6.1 (4.8-8.9) 59% had prostatectomy GS of 7 61% had positive surgical margins 33% had seminal vesicle invasion CAPRA-S Intermediate risk score (3-5): 60.7% (136) 12/224 experienced clinical recurrence 68 had biochemical recurrence 34 experienced salvage treatment failure. **Recurrence rates by Decipher risk category at 10-y post prostatectomy:** Decipher low score: 2.6% vs 13.6% for average to high score (P=0.02) **Discrimination accuracy for clinical recurrence measured by C-index:** Decipher: 0.8 (0.64 – 0.92) CAPRA-S: 0.73 (95% CI 0.49 – 0.95) CAPRA-S + Decipher: 0.84 (C-index increased by 0.11). Multivariate analysis for clinical recurrence: Decipher score: HR 1.48 (1.09 – 2.01), **P=0.01** CAPRA-S: HR 1.27 (0.97 – 1.66), P=0.08	conventional pathological predictors. This may help providers to add other tx to patients classified as high risk of recurrence by Decipher. RoB: Retrospective design, moderate to small sample size, inherent limitations to retrospective design, there were few numbers of end points, this cohort of patients was predominantly white Of note, white is predominant in all the studies.
Clinical utility			
Authors: (Marascio et al., 2020) Aim: to determine the impact of GC testing on postoperative management in men with prostate cancer post prostatectomy. Country: USA	Design: registry based study There were two cohorts: the clinical utility & clinical benefit cohorts N= 3910 (n=3455 in the adjuvant and n=455 in salvage), N=102 respectively Inclusion criteria: pathological stage ≥pT3 or positive margins; providers must be certified for using GC. Patients were required to have undetectable PSA after RP and harbor one or more AP features (positive surgical margins or pT3 disease).	**Patient's characteristics:** Patients with adverse features (≥pT3 or positive margins) post prostatectomy who underwent decipher testing. There were two cohorts: the clinical utility & clinical benefit cohorts NO significant difference was reported btw the cohorts. Age: 63 – 69 y Race: Pre-operative PSA: 6.9 GS: Clinical stage: RP grade groups: Majority in both cohorts had GG2 or GG3	The utilization of GC significantly influenced treatment recommendations with a number needed to test of 3. GC may be used in clinical practice. Limitations: Only 58% had both pre & post GC provider tx recommendations. There is lack of follow-up data in

<table>
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<td>Exclusion criteria: Patients with lymph node positive or
metastatic disease at diagnosis or patients who had received neoadjuvant therapy.

Index test: Decipher genomic classifier

Comparator:

Follow-up: 22 months in clinical benefit cohort, not available in clinical utility cohort

Primary outcome: early BCR within 2-year post-RP (BCR defined as PSA ≥ 0.2 ng/mL after achieving nadir (<0.1 ng/ml)).

Other: Time to BCR; Influence of the GC test on treatment
decision-making in adjuvant setting</td>
<td>Pathology T stage: majority in both cohorts were pT3a or pT4b
Positive margins: majority had positive margins

GC risk group: In the clinical benefit cohort, most patients were high-risk GC. In the clinical utility cohort, most patients were low & intermediate risk.

Findings:
GC classified 28, 24, and 48% as low- (GC < 0.45), intermediate-(0.45–0.60), and high- (>0.60) genomic-risk, respectively.
These suggest a 5-year metastasis rate of < 4%, 4–9% and > 9%, respectively.

Change in tx recommendations
<table>
<tr><th>Provider Recommendations</th><th>Pre-GC</th><th>Post GC</th></tr>
<tr><td>Observation + PSA monitoring</td><td>69%
(n = 1384),</td><td>Increased to 75%</td></tr>
<tr><td>ART</td><td>25% (n = 501)</td><td>Decreased to 14%</td></tr>
<tr><td>ART + ADT</td><td>5%
(n = 92)</td><td>Increased to 9%</td></tr>
<tr><td>adjuvant ADT alone</td><td>1% (n=25)</td><td>Increased to 2%</td></tr>
<tr><td colspan="2"></td><td>P for all <0.001
Tx changed for 39% of patients
NNT of 3 to change one tx decision</td></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td></tr>
</table>
Tx was intensified or de-intensified for 18 and 21% of adjuvant cases, and 30 and 14% of salvage cases.

High GC score was significantly associated with intensification of therapy [8.7 (5.4–13.8) <0.001].

Clinical benefit cohort:
61% had high risk GC. Among those who received the recommended adjuvant radiation therapy (ART), 2% had 2-year PSA recurrence; 25% had 2-year PSA recurrence among those who did not receive the recommended ART [(HR 0.1 [95% CI 0.0-0.6], p = 0.013)].

In low & intermediate risk GC, 93% followed
the recommendation for observation with PSA monitoring. The 2-year PSA recurrence was comparable btw those who followed the recommendation and those who received ART.</td>
<td>the clinical utility cohort. There was no control group.

Overall, risk of bias is high.</td>
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<td>(Gore et al., 2017)

Aim: evaluated the impact of the Decipher test on decision-making for ART and SRT</td>
<td>Design: prospective study

N=265 (n=150 for ART, n=115 for SRT)

Two cohorts were used: ART & SRT arms.

Inclusion criteria: “Patients had prostate cancer</td>
<td>Patient’s characteristics

Patients had prostate cancer that was previously treated with radical prostatectomy and had adverse pathologic features and were being considered for either ART or SRT.

Median Age: 63 - 64
Race:</td>
<td>Conclusion:
Decipher test may significantly impact treatment change in this population.</td>
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<td>Country:</td>
<td>that was previously treated with radical prostatectomy and
were being considered for either ART or SRT. men with pathologically non-organ-confined prostate cancer (ie, pathological classification of T3 disease, including men with extraprostatic extension and/or seminal vesicle invasion) or positive surgical margins into the ART arm. Patients who were eligible for ART were required to have undergone surgery within the preceding 12 months. Patients with a PSA increase or definite biochemical disease
recurrence (BCR), defined as a PSA 0.2 ng/mL with a confirmatory reading, were enrolled into the SRT
arm. Patients who were eligible for SRT were allowed to
have received adjuvant hormone therapy before their
BCR”.

Exclusion criteria: Patients with metastatic disease. Failure of
PSA to nadir to ≤0.1 ng/mL within 3 months of surgery,
receipt of neoadjuvant androgen deprivation therapy
(ADT) or, for patients in the ART arm, the receipt of
adjuvant systemic therapy.

Intervention: Decipher GC

Comparator: clinical variables/before and after GC

Follow-up: NR

Primary outcome: to determine whether Decipher impacts treatment recommendations after RP and at time of BCR.</td>
<td>Pre-operative PSA: 6.3 – 6.7
GS:
Clinical stage:

RP grade groups:
Pathology T stage: most patients were T2 & T3a
Positive margins: half of the patients in the ART arm and near half of patients in the SRT group had positive margins
GC risk group: In the ART group, Decipher classified 46% as low risk and 32% as high risk. In the SRT arm, Decipher classified 33% as low risk and 41.7% as high risk.
94 & 91% completed the before and after GC visit.

Findings:
<table>
<tr><th>Recommendations</th><th colspan="3">ART</th><th colspan="3">SRT</th></tr>
<tr><td></td><td>PreGC</td><td>PostGC</td><td>Change</td><td>PreGC</td><td>PostGC</td><td>Change</td></tr>
<tr><td></td><td></td><td></td><td>18% overall change</td><td></td><td></td><td>32% overall change</td></tr>
<tr><td>Observation</td><td>88% (133)</td><td></td><td></td><td>58% (n=67)</td><td></td><td></td></tr>
<tr><td>Observation</td><td>91% of ART and Decipher low-risk</td><td>96% of ART and Decipher low-risk</td><td></td><td></td><td></td><td></td></tr>
<tr><td>ART</td><td>11% (n=17)</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>SRT</td><td></td><td></td><td></td><td>32% (n=37)</td><td></td><td></td></tr>
<tr><td>ADT
or SRT and ADT</td><td></td><td></td><td></td><td>9% (n=11)</td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
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Stratified by Decipher risk group in ART cohort:
<table>
<tr><td>Recommendations</td><td colspan="2">Decipher Low-risk</td><td colspan="2">Decipher Intermediate risk</td><td colspan="2">Decipher high -risk</td></tr>
<tr><td></td><td>Pre-GC</td><td>Post-GC</td><td>Pre-GC</td><td>Post-GC</td><td>Pre-GC</td><td>Post-GC</td></tr>
<tr><td>Observation</td><td>91%</td><td>96%</td><td>79%</td><td>73%</td><td>92%</td><td>63%</td></tr>
<tr><td>more intense therapy (ART instead
of observation or ART and ADT instead of RT alone)</td><td></td><td></td><td></td><td></td><td>8%</td><td>37%</td></tr>
</table>
Stratification by Decipher risk group in SRT cohort:
<table>
<tr><td>Recommendations</td><td colspan="2">Decipher Low-risk</td><td colspan="2">Decipher Intermediate risk</td><td colspan="2">Decipher high -risk</td></tr>
<tr><td></td><td>Pre-GC</td><td>Post-GC</td><td>Pre-GC</td><td>Post-GC</td><td>Pre-GC</td><td>Post-GC</td></tr>
</table></td>
<td>RoB: High (confounders, SRT arm had small sample size, there was no control group,, this is an interim report for whom tx recommended may not represent actual tx).</td>
</tr>
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<table>
<tr><td>Observation</td><td>63%</td><td>74%</td><td>55%</td><td>59%</td><td>%</td><td>%</td></tr>
<tr><td>more intense therapy (SRT instead of observation, SRT and ADT instead of RT alone, or ADT)</td><td></td><td></td><td></td><td></td><td>69%</td><td>44%</td></tr>
</table>

Association between Decipher & treatment change:
There is significant association btw Decipher & treatment change after adjusting for demographic, clinical, and pathological variables. In ART, OR was 1.48 (1.19-1.85), P<.001. In SRT, OR was 1.30 (1.03-1.65), P=0.03.

Decision effectiveness:
The use of the Decipher test was associated with decreased decisional conflict overall.
In ART arm, decisional conflict was reduced from 25 before GC to 19 after GC (P<0.001).
In the SRT cohort, decisional conflict decreased from 27 to 23 (P<0.001).
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<td>(Michalopoulos et al., 2014)

Aim: To assess the effect of an individualized genomic classifier (GC) test, for predicting metastasis following radical prostatectomy (RP), on urologists' adjuvant treatment decisions when caring for high-risk patients.</td>
<td>Design: prospective study
N=146
Intervention: Decipher GC

Comparator: before and after GC</td>
<td>Patients' characteristics:
Patients had prostate cancer with adverse pathologic features following RP (pathologic stage pT3 or positive surgical margins.
Age: 63
Preoperative PSA: <10 ng/mL

GC reclassified 60% of high-risk patients as low-risk.

Tx recommendations change occurred in 31% of patients.

After GC test, 42.5% of patients who were initially recommended adjuvant therapy were recommended to undergo observation.

GC risk was a significant predictor of treatment recommendations (OR = 4.04; 95% CI = 2.36, 6.92; p < 0.0001). It was the only predictor.

Decisional conflict: With the use of Decipher GC, there was les decisional conflict with regard to adjuvant tx decisions (P<0.001).</td>
<td>This study demonstrated that Decipher may influence treatment recommendations in post-RP patients with high risk of metastasis. It may guide adjuvant therapy. Decisional conflict regarding adjuvant therapy may decreased with the use of GC.

Rob: High (small sample size,).</td>
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Other studies

Decipher using biopsy:

(Press et al., 2022): This was a retrospective cohort study among patients with low- and favorable intermediate-risk prostate cancer on active surveillance who underwent biopsy-based Decipher testing. The authors included 133 patients with a median age of 67.7 yr and median prostate-

specific of 5.6 ng/ml. 75.9% had GG1 and 24.1% had GG2 disease. Decipher score was significantly associated with biopsy upgrading (OR 1.37 (1.05-1.79; p = 0.02)). The Decipher score was associated with upgrading among patients with biopsy GG 1 disease, but not GG2 disease.