

# Active Surveillance Use Among a Low-risk Prostate Cancer Population in a Large US Payer System: 17-Gene Genomic Prostate Score Versus Other Risk Stratification Methods

Steven Canfield, MD,<sup>1</sup> Michael J. Kemeter, MSPAS,<sup>2</sup> John Hornberger, MD, MS,<sup>2</sup> Phillip G. Febbo, MD<sup>2</sup>

<sup>1</sup>Division of Urology, University of Texas Health Science Center, Houston, TX; <sup>2</sup>Genomic Health, Inc., Redwood City, CA

Many men with low-risk prostate cancer (PCa) receive definitive treatment despite recommendations that have been informed by two large, randomized trials encouraging active surveillance (AS). We conducted a retrospective cohort study using the Optum™ Research Database (Eden Prairie, MN) of electronic health records and administrative claims data to assess AS use for patients tested with a 17-gene Genomic Prostate Score™ (GPS; Genomic Health, Redwood City, CA) assay and/or prostate magnetic resonance imaging (MRI). De-identified records were extracted on health plan members enrolled from June 2013 to June 2016 who had  $\geq 1$  record of PCa ( $n = 291,876$ ). Inclusion criteria included age  $\geq 18$  years, new diagnosis, American Urological Association low-risk PCa (stage T1-T2a, prostate-specific antigen  $\leq 10$  ng/mL, Gleason score = 6), and clinical activity for at least 12 months before and after diagnosis. Data included baseline characteristics, use of GPS testing and/or MRI, and definitive procedures. GPS or MRI testing was performed in 17% of men (GPS,  $n = 375$ , 4%; MRI,  $n = 1174$ , 13%). AS use varied from a low of 43% for men who only underwent MRI to 89% for GPS-tested men who did not undergo MRI ( $P < .001$ ). At 6-month follow-up, AS use was 31.0% higher (95% CI, 27.6%-34.5%;  $P < .001$ ) for men receiving the GPS test only versus men who did not undergo GPS testing or MRI; the difference was 30.5% at 12-month follow-up. In a large US payer system, the GPS assay was associated with significantly higher AS use at 6 and 12 months compared with men who had MRI only, or no GPS or MRI testing.

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## KEY WORDS

Prostate cancer • Active surveillance • Evidence-based practice • Comparative effectiveness research • Genomic biomarker • Magnetic resonance imaging

Guidelines from the National Comprehensive Cancer Network (NCCN) and American Urological Association (AUA) encourage active surveillance (AS), also referred to as watchful waiting, expectant management, or deferred treatment, as a preferred management option for men with low-risk prostate cancer (PCa).<sup>1,2</sup> The guidelines reference peer-reviewed evidence on rates of mortality and metastatic disease, incidence of procedure-related adverse events, and patients' quality of life from randomized trials, combined with a preponderance of supportive evidence from prospective, observational studies.

Several studies reveal trends and variations in AS use among men seen in real-world settings. In an analysis using the National Cancer Database, Løppenberget and associates<sup>3</sup> assessed 115,208 men diagnosed with clinically low-risk PCa between 2010 and 2014 and found that 14,180 (12.3%) were initially managed by AS. Use of AS varied between 0% and 100%, with more than 58% of the variation associated with patient-level factors, such as age, race, stage, prostate-specific antigen (PSA) level, and comorbidities. Approximately 10% of the variation in AS use was associated with nonmedical factors, such as treatment facility type or facility volume. In another study, using the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) national registry, Cooperberg and Carroll<sup>4</sup> reported that surveillance use for clinically low-risk disease (Cancer of the Prostate Risk Assessment

[CAPRA] score range, 0-2) was <15% from 1990 through 2009, and increased in 2010 through 2013 to 40%. The Michigan Urological Surgery Improvement Collaborative (MUSIC), a consortium of 43 academic and community urology practices, reported AS use among 2643 men diagnosed with low-risk PCa between 2012 and 2016.<sup>5</sup> Investigators reported a median AS use of 57% (range 30%-73%), an increase relative to prior studies that they attributed to implementing focused quality improvement initiatives.

Attempts to further increase guideline adherence have included healthcare system integration (eg, accountable care organizations), payment reforms, clinical pathways, clinical report cards, and staff training on shared-medical decision making.<sup>6-10</sup> For example, Ehdaie and associates<sup>11</sup> enlisted five physicians for a 1-hour training session on counselling patients on the implications of AS. They enrolled 1003 low-risk patients

increase guideline-adherent AS use in men with clinically low-risk PCa.<sup>12,13</sup> The Oncotype DX® Genomic Prostate Score™ (GPS; Genomic Health, Redwood City, CA) is a 17-gene molecular assay performed on formalin-fixed, paraffin-embedded diagnostic prostate biopsy samples. The expression of 12 cancer-related genes from 4 molecular pathways is normalized to the expression of 5 reference genes. A GPS result is indexed to the patient's NCCN risk category to produce an estimated likelihood for high-grade disease and/or non-organ-confined disease. The GPS assay was clinically validated as an independent predictor of adverse pathology, biochemical recurrence after prostatectomy, metastases, and prostate-specific death in men with clinically low-risk disease.<sup>14-17</sup> Three prior studies have demonstrated that GPS testing is associated with an absolute 21% to 29% difference in AS use compared with baseline (non-GPS testing).<sup>18-20</sup> GPS testing

*Individualized, objective risk stratification using molecular biomarkers and multiparametric prostate magnetic resonance imaging (MRI) have been assessed as potential solutions to further increase guideline-adherent AS use in men with clinically low-risk PCa.*

(761 before training, 242 after) and found a modest, nonsignificant increase in AS use (9.1%; 95% CI, -0.4 to 19.4%).

Individualized, objective risk stratification using molecular biomarkers and multiparametric prostate magnetic resonance imaging (MRI) have been assessed as potential solutions to further

is discussed in the NCCN guidelines as an option for improved risk stratification for men with early stage PCa.<sup>2</sup> Prostate MRI and genomic testing with the GPS assay have shown weak correlation, suggesting that the two modalities represent independent predictors.<sup>13</sup> Guidelines conclude MRI may be useful for integration

into clinical staging, especially among men with Gleason score  $\geq 7$ , but its role in low-risk PCa remains investigational.<sup>2,21</sup>

Our primary aim was to estimate AS use in a large US payer system in men with low-risk PCa who received GPS testing, MRI imaging, or no testing by either GPS testing or MRI. We also assessed the effect of GPS testing and/or MRI on AS use, changes by year of diagnosis, and level of AS use between 6- and 12-month follow-up.

## Methods

### Data Sources

A retrospective cohort study was conducted using the Optum<sup>TM</sup> Research Database (ORD; Eden Prairie, MN), which includes electronically stored medical records and administrative claims data linked to enrollment information and laboratory data from a large US health insurer offering both commercial and Medicare Advantage health plans. The ORD includes more than 34 million persons per year who are geographically diverse across the United States, with the greatest proportion in the Midwest and South US Census Bureau regions. The age and sex distribution of the enrollees is similar to that reported by the US Census Bureau for both the commercially insured and the Medicare managed care populations. The insurer provides coverage for physician, hospital, and prescription drug services. The use of the ORD as a data source for real-world, comparative effectiveness research has been described previously.<sup>22,23</sup>

De-identified records stripped of identifiable protected health information was extracted or accessed during the study in compliance with the US Health Insurance Portability and Accountability Act.

### Patient Selection

De-identified records were extracted for patients enrolled in the health plan from January 2013 to June 2016 who had  $\geq 1$  record of PCa using the International Classification of Diseases (ICD)-9 185 and ICD-10 C61 diagnostic codes. Inclusion criteria included age  $\geq 18$  years, AUA low-risk PCa (stage T1-T2a, PSA  $\leq 10$  ng/mL, Gleason score = 6), clinical activity for at least 12 months before and 6 months after diagnosis, and at least 1 PSA measurement within 12 months before or after diagnosis. PCa diagnosis date was defined as the patient's earliest observed PCa diagnosis (no record of a diagnosis 12 months prior or during the observational window). Because the GPS assay became commercially available in June 2013, we restricted our analysis to records of patients enrolled in the database from June 2013 to June 2016. Records from GHI were submitted to the ORD for linkage to assure identification of the patients who had GPS testing. Patients with American Medical Association's Current Procedural Terminology<sup>®</sup> (CPT) codes for genomic tests that were not the GPS assay were excluded because the small number of patients ( $n = 40$ ) precluded meaningful comparisons with other groups.

### Study Measures

Baseline patient characteristics included age at diagnosis, year

of the test's name and measurement. For example, "test name = *prostate-specific antigen*, measurement type = *Gleason*." PCa-related procedures were recorded for patients in the cohort at 6 and 12 months of follow-up, and included radical prostatectomy, radiation therapy, brachytherapy, cryotherapy, or hormone therapy (Table 1). A PCa-related procedure was reported if the patient had only one procedure during the 6- or 12-month follow-up period. A patient with more than one procedure over the interval was designated as having had multiple procedures. A patient with no recorded PCa-related procedures was designated as having undergone AS.

### Data Management and Analysis

Summary statistics for all variables were reported from the ORD; number of patients and frequencies were reported for categorical variables, and means and standard deviations were reported for continuous variables. Subsequent data management and analyses were performed using STATA<sup>®</sup> 15/IC 15.1 for Windows (StataCorp LLC, College Station, TX).

A Pearson  $\chi^2$  test was performed (2-sided,  $\alpha = 0.05$ ) to assess differences, unadjusted by covariates, in frequency of AS use by test utilization. Multivariate logistic regression of AS use was performed to control further for variations in baseline covariates; postestimation

*The primary analysis was to assess the difference in AS use by test utilization adjusted for baseline covariates. Increasing age was significantly associated with AS use.*

of diagnosis, census geographic region, insurance status, and number of comorbidities. Genomic testing was recorded using the CPT codes 84999, 81479, and/or 81599. Other tests were based on

predictive margins are reported using confidence intervals computed by delta method.<sup>24,25</sup> The primary analysis was to assess the difference in AS use by test utilization adjusted for baseline covariates.

**TABLE 1****List of CPT, HCPCS, or ICD Codes for Procedures**

|  |   |
|--|---|
| Prostatectomy or radical prostatectomy | CPT4: 52647, 52648, 52649, 53850, 53852, 55801, 55810, 55812, 55815, 55821, 55831, 55840, 55842, 55845, 55866, 55873, 51597, 52601, 52612, 52614, 52630, 53853, 55801, 55810, 55812, 55815, 55821, 55831, 55840, 55842, 55845, 55866, 55899<br>ICD9: 60.21, 60.29, 60.3, 60.4, 60.5, 60.62, 60.69, 60.96, 60.97   |
| Radiation                              | CPT4: 77401, 77402, 77403, 77404, 77406, 77407, 77408, 77409, 77411, 77412, 77413, 77414, 77416, 77418, 77422, 77423, 77520, 77522, 77523, 77525, 77750, 77373, 77380, 77381, 77425, 77427, 77431, 77432, 77435, 77499, 77331, 77336, 77370, 77011, 77417, 77421, 77470, 0197T, 55876, 76370, 76950, 76965, 77014, 77261, 77262, 77263, 77280, 77285, 77290, 77295, 77299, 77300, 77301, 77305, 77310, 77315, 77321, 77332, 77333, 77334, 77338, 77399, 77422, 77423, 77520, 77522, 77523, 77525, 77750, 77373, 77380, 77381, 77425, 77427, 77431, 77432, 77435, 77499, 77331, 77336, 77370, 77011, 77417, 77421, 77470, 0197T, 55876, 76370, 76950, 76965, 77014, 77261, 77262, 77263, 77280, 77285, 77290, 77295, 77299, 77300, 77301, 77305, 77310, 77315, 77321, 77332, 77333, 77334, 77338, 77399, 77401, 77402, 77403, 77404, 77405, 77406, 77407, 77408, 77409, 77410, 77411, 77412, 77413, 77414, 77415, 77416, 77417, 77418<br>HCPCS: G0173, G0339, S8049<br>ICD9: 92.21, 92.22, 92.23, 92.24, 92.25, 92.26, 92.29, 92.30, 92.31, 92.32, 92.33, 92.39, 92.41 |
| Cryotherapy                            | CPT4 55873  |
| Hormone                                | CPT4: 54520, 54640, 54650, 96374, 54690<br>HCPCS: J9155, S0175, J1950, J9217, J9218, J9219, J9202, J3315<br>ICD9: 92.27, 92.28, 92.20   |

CPT, Current Procedural Terminology; HCPCS, Healthcare Common Procedure Coding System; ICD, International Classification of Diseases.

Secondary analyses included assessing differences stratified by the year patients were enrolled in the database and between the 6- and 12-month follow-up periods. We also assessed the distribution of procedures—prostatectomy, radiation therapy, and other (cryotherapy, brachytherapy, hormone therapy, or multiple therapies)—by GPS and/or MRI testing.

## Results

Screening identified 290,163 patients with one or more electronic health record (EHR) PCa records between June 2013 and June 2016 (Figure 1). Applying inclusion/exclusion criteria and linking records between ORD and GHI resulted in an analysis population of 8920 patients. Table 2 shows the distributions of covariates, by cohorts

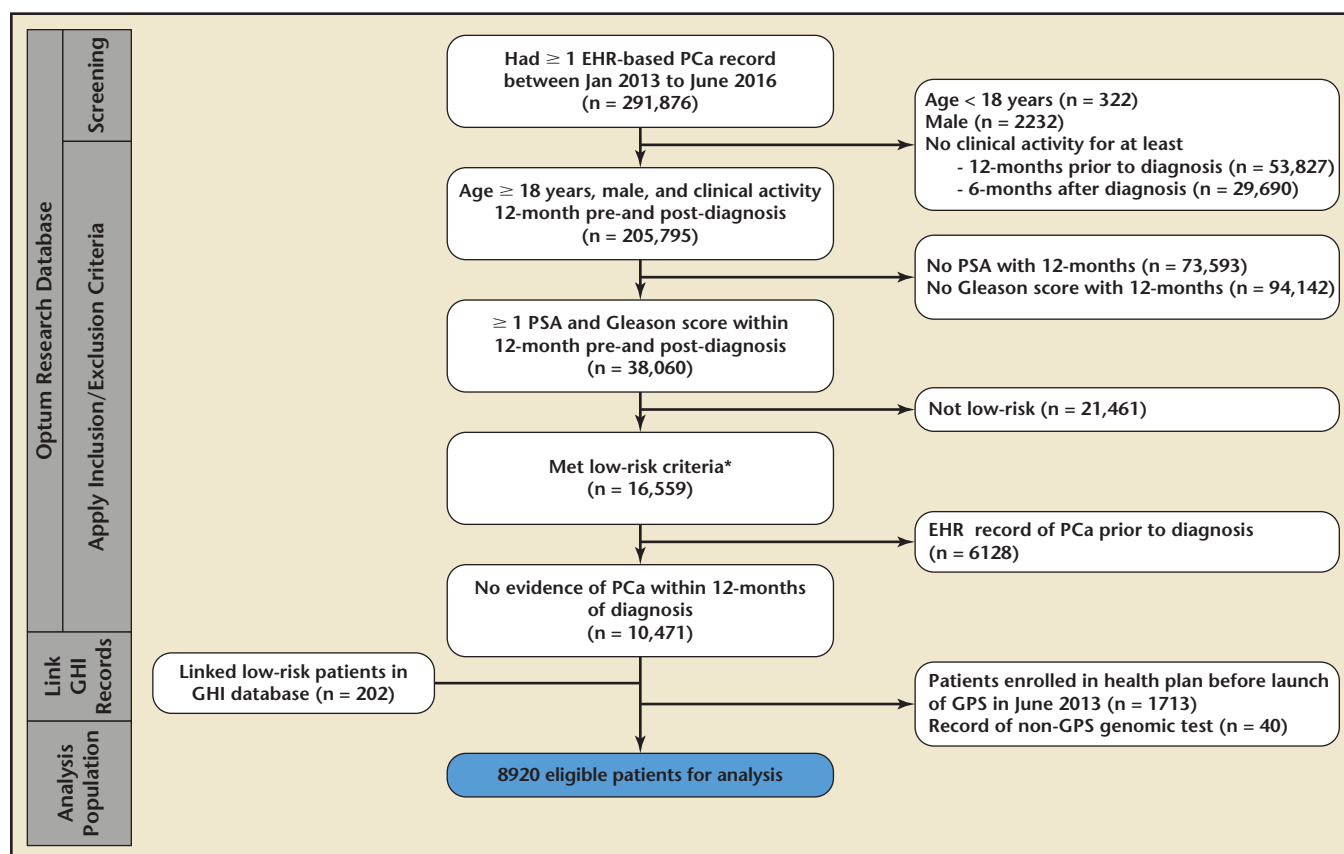
of patients who had 6 or 12 months of follow-up; 81% of men followed to 6 months had follow-up recorded up to 12 months. Among men with 6 months of follow-up, 375 had GPS testing (300 had only GPS testing and 75 had GPS testing plus MRI); 1099 patients had MRI only.

The frequency of AS use significantly varied among different combinations of GPS and MRI testing from a low of 42% for MRI only at 12 months of follow-up to 89% for GPS testing only (Figure 2; Pearson  $\chi^2 = 245$ ,  $P < .001$ ). Among patients followed for 6 months, AS utilization was 31.2% higher (95% CI, 22.6% to 39.7%;  $P < .001$ ) in patients undergoing GPS testing only versus patients who did not receive GPS testing or MRI (Table 3, Figure 3). AS use was 5.1% (95% CI, -9.9% to 20.0%;  $P = \text{NS}$ ) higher among patients undergoing MRI than

among those who had neither GPS nor MRI. Combined GPS and MRI testing also correlated with significantly higher AS use, which was similar to the effect for patients with GPS testing only. AS use declined by 3.2% (95% CI, -4.7% to -1.7%,  $P < .001$ ) between the 6- and 12-month follow-up periods.

Increasing age was significantly associated with AS use (Table 2; 7.8% increase per year; 95% CI, 3.4% to 12.3%;  $P < .001$ ). No significant differences in AS use were detected based on region, insurance status, or baseline symptoms/diagnosis. Other than in 2013, AS use was stable between 2014 and 2016 in each of the groups identified (Figure 4). Prostatectomy was the most common procedure (22%) among men who did not receive GPS testing or MRI (Figure 5), compared with 5% use of radiation therapy and





**Figure 1.** From screening to analysis population. The NCCN guidelines define low-risk prostate cancer as follows: clinical stage T1 to T2a, Gleason score 6, and PSA level <10 ng/mL. EHR, electronic health record; GHI, Genomic Health (Redwood City, CA); NCCN, National Comprehensive Cancer Network; NCDB, National Cancer Database; PCa, prostate cancer; PSA, prostate-specific antigen.

4% for other procedures (cryotherapy, brachytherapy, hormone therapy, or multiple procedures). Prostatectomy was >70% less common with GPS testing relative to no GPS testing or MRI. In contrast, radiation therapy was more than twice as common for patients with MRI only compared with no GPS testing, no MRI, and all other testing groups ( $P < .001$ ).

## Discussion

The use of AS was significantly higher among patients undergoing GPS testing compared with MRI

adjustment by cohort year or differences in mean covariate levels, or whether AS use was assessed at 6 or 12 months. The level of AS use declined between 6 and 12 months by 3.2%. MRI was the most common test ordered (13%) and was associated with lower AS use and higher use of radiation therapy, compared with GPS testing or with no GPS or MRI testing.

Our findings are consistent with previous studies of the effect of GPS testing on AS use (Table 4). Dall'Era and colleagues<sup>20</sup> showed that men with low-risk disease (n = 124) who

alone. Albala and colleagues<sup>19</sup> compared 180 men (100 identified retrospectively without testing and 80 followed prospectively who underwent testing) and found a 21% absolute increase in AS utilization for NCCN very low- and low-risk patients. In a prospective study of physician management change (recommendation pretesting versus actual treatment after testing), Eure and coworkers<sup>18</sup> found that AS use was 22% higher than it would have been without the additional information from GPS testing. The baseline rate of AS in these three studies varied between 38% and 43%.

Our study is one of the largest investigations into AS utilization in an unselected (real-world) population and included a study design that permitted assessment and control for baseline characteristics and changes in patterns of care over time. We

*The use of AS was significantly higher among patients undergoing GPS testing compared with MRI or with no GPS or MRI testing.*

or with no GPS or MRI testing. The difference in AS use with GPS testing versus no GPS or MRI testing was stable regardless of

underwent GPS testing had a 24% higher rate of AS use compared with untested men with similar risk based on clinicopathologic factors

**TABLE 2****Baseline Characteristics (Age, Region, Insurance Status, Other Diagnosis) and Procedures Used During the Follow-up Period**

| Covariate                                      | Follow-up Period       |      |                         |      |
|--|------------------------|------|-------------------------|------|
|  | 6 mo (%)<br>(n = 8920) |      | 12 mo (%)<br>(n = 7201) |      |
| Age, n (%)                                     |                        |      |                         |      |
| ≤50 y  | 190                    | (2)  | 143                     | (1)  |
| 50–59 y  | 1903                   | (21) | 1493                    | (20) |
| 60–64 y  | 1825                   | (20) | 1478                    | (20) |
| 65–69 y  | 1993                   | (22) | 1612                    | (22) |
| 70–79 y  | 2435                   | (27) | 1988                    | (27) |
| ≥80 y  | 574                    | (6)  | 487                     | (6)  |
| Region, n (%)                                  |                        |      |                         |      |
| Northwest                                      | 1184                   | (13) | 915                     | (12) |
| Midwest  | 4737                   | (53) | 3861                    | (53) |
| South  | 2097                   | (23) | 1717                    | (23) |
| West   | 811                    | (9)  | 634                     | (8)  |
| Other or missing                               | 91                     | (1)  | 74                      | (1)  |
| Insurance status, n (%)                        |                        |      |                         |      |
| Commercial                                     | 3901                   | (43) | 3135                    | (43) |
| Medicare                                       | 2415                   | (27) | 1992                    | (27) |
| Medicaid                                       | 106                    | (1)  | 74                      | (1)  |
| Uninsured                                      | 598                    | (6)  | 527                     | (7)  |
| Multiple                                       | 1197                   | (13) | 964                     | (13) |
| Other or missing                               | 703                    | (7)  | 509                     | (7)  |
| Test, n (%)                                    |                        |      |                         |      |
| No test  | 7446                   | (83) | 5755                    | (79) |
| Only GPS                                       | 300                    | (3)  | 202                     | (2)  |
| Only MRI                                       | 1099                   | (12) | 1170                    | (16) |
| GPS & MRI                                      | 75                     | (0)  | 74                      | (1)  |
| Baseline clinical diagnoses or symptoms, n (%) |                        |      |                         |      |
| Selected urologic symptoms <sup>a</sup>        | 2605                   | (29) | 2183                    | (30) |
| Other diagnoses <sup>b</sup>                   | 1407                   | (15) | 1114                    | (15) |
| Procedure, n (%)                               |                        |      |                         |      |
| Brachytherapy                                  | 327                    | (3)  | 349                     | (4)  |
| Cryotherapy                                    | 23                     | (0)  | 11                      | (0)  |
| Hormone therapy                                | 12                     | (0)  | 11                      | (0)  |
| Multiple therapies                             | 826                    | (9)  | 860                     | (11) |
| No observed therapy                            | 5258                   | (58) | 3962                    | (55) |
| Prostatectomy                                  | 1957                   | (21) | 1589                    | (22) |
| Radiation                                      | 517                    | (5)  | 419                     | (5)  |

In all, 40 patients were excluded who had a different genomic test (not otherwise specified).

<sup>a</sup>Erectile dysfunction, incontinence, cystitis, proctitis.<sup>b</sup>History of malignant neoplasm or symptoms or involving respiratory system and other chest symptoms.

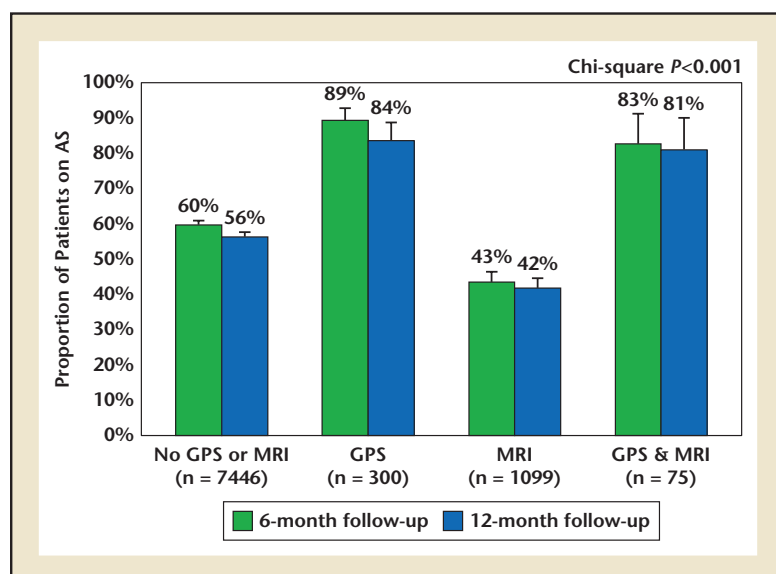


Figure 2. Proportion of AS use by 6- and 12-month follow-up period (mean + 95% CI). AS, active surveillance; GPS, Genomic Prostate Score (Genomic Health, Redwood City, CA); MRI, magnetic resonance imaging.

found a slightly greater association of GPS testing with AS use compared with previous studies (by an absolute difference of 6%-9%). We also found that the effect of GPS testing on AS use was stable over time, and that AS rates among those without GPS or MRI testing remained relatively unchanged from 2014 to 2016. Because of our contemporaneous study design (patients who underwent GPS testing versus those who did not receive testing in the same year and over multiple-year cohorts), the absolute effects seen herein are not likely a result of time bias.

We found that 17% of patients with low-risk PCa underwent some evaluation with GPS testing or MRI

**TABLE 3**

**Effect of Covariate Adjustment on Predictive Margins of the Difference on Active Surveillance Use From Baseline**

| Covariate                               | Difference (from ref.) (%) | SE (%) | 95% CI (%) |      |   |
|---|----------------------------|--------|------------|------|---|
|   |                            |        | Low        | High |   |
| Testing                                 |                            |        |            |      |   |
| GPS                                     | 31.2                       | 4.3    | 22.6       | 39.7 | a |
| MRI                                     | 5.1                        | 7.6    | −9.9       | 20.0 |   |
| GPS & MRI                               | 30.4                       | 5.4    | 19.9       | 40.9 |   |
| No GPS or MRI                           | − ref −                    |        |            |      |   |
| Region                                  |                            |        |            |      |   |
| Northeast                               | 1.1                        | 2.2    | −3.3       | 5.5  |   |
| Midwest                                 | 1.0                        | 2.2    | −3.3       | 5.3  |   |
| South                                   | 1.5                        | 2.4    | −3.1       | 6.2  |   |
| West                                    | 1.3                        | 2.4    | −3.3       | 6.0  |   |
| Other or missing                        | − ref −                    |        |            |      |   |
| Insurance                               |                            |        |            |      |   |
| Commercial                              | 0.03                       | 0.5    | −1.0       | 1.0  |   |
| Medicare                                | −0.2                       | 0.8    | −1.8       | 1.3  |   |
| Medicaid                                | −2.7                       | 2.0    | −6.5       | 1.1  |   |
| Uninsured                               | 0.7                        | 0.8    | −0.1       | 2.3  |   |
| Multiple                                | −0.1                       | 0.1    | −2.4       | 0.4  |   |
| Other                                   | − ref −                    |        |            |      |   |
| Other covariates                        |                            |        |            |      |   |
| Age, y                                  | 7.8                        | 2.3    | 3.4        | 12.3 | a |
| Selected urologic symptoms <sup>b</sup> | −0.7                       | 0.3    | −1.2       | −0.2 |   |
| Other diagnoses <sup>c</sup>            | −0.2                       | 0.4    | −1.0       | 0.5  |   |

GPS, Genomic Prostate Score (Genomic Health, Redwood City, CA); MRI, magnetic resonance imaging; SE, standard error.

<sup>a</sup> $P < .001$ .

<sup>b</sup>Erectile dysfunction, incontinence, cystitis, proctitis.

<sup>c</sup>History of malignant neoplasm or symptoms or involving respiratory system and other chest symptoms.

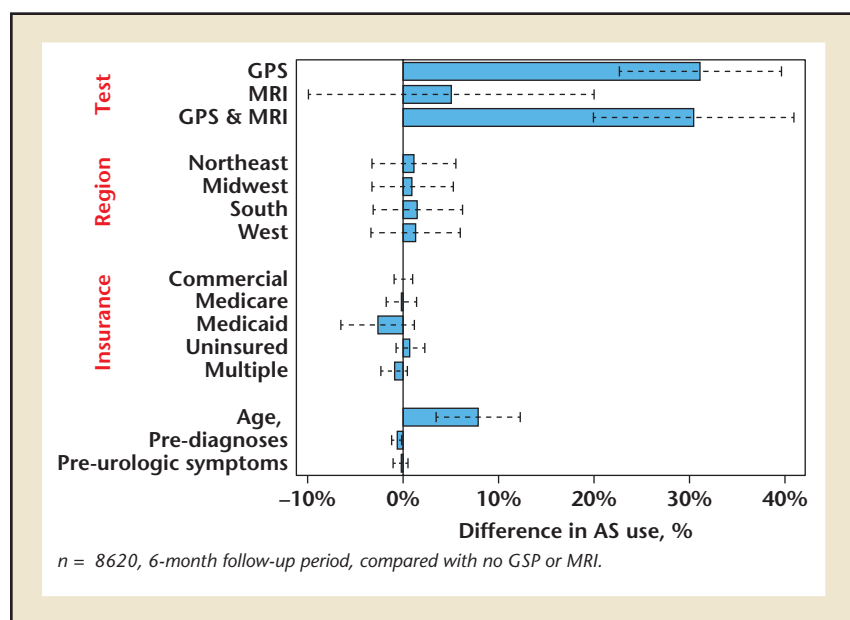


Figure 3. Effect of covariate adjustment on predictive margins of difference on active surveillance use. AS, active surveillance; GPS, Genomic Prostate Score (Genomic Health, Redwood City, CA); MRI, magnetic resonance imaging.

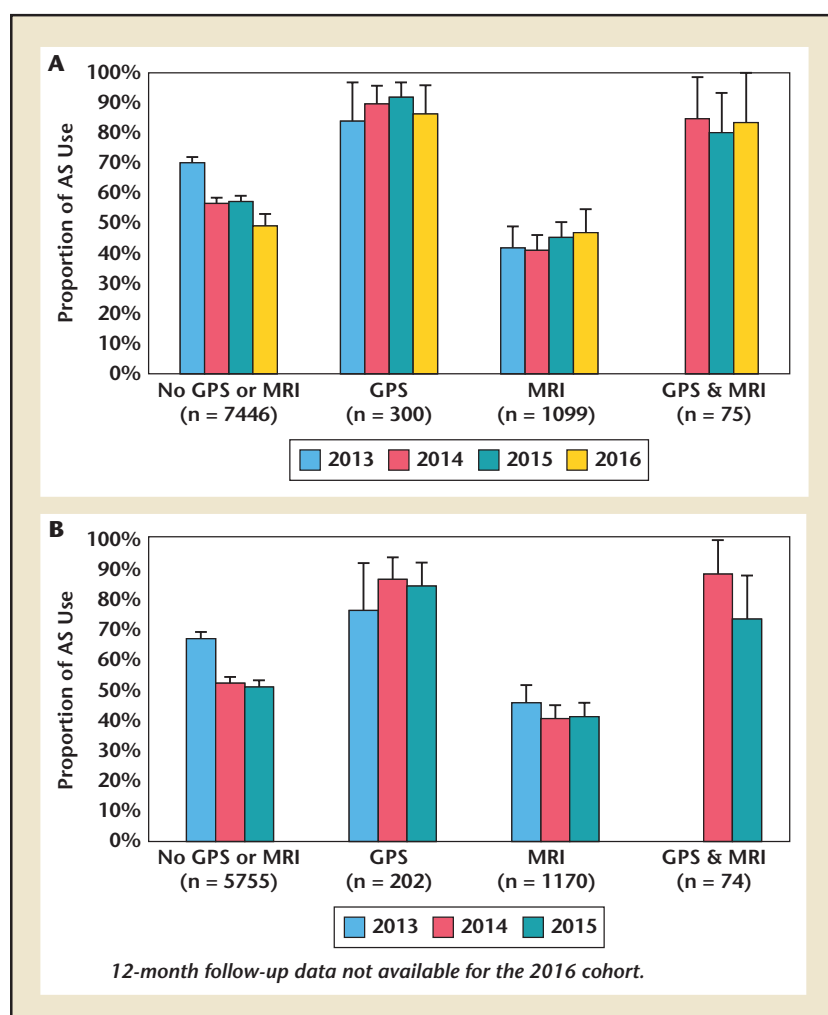


Figure 4. Proportion of active surveillance use by follow-up (A: 6 mo, B: 12 mo), stratified by year (mean + 95% CI). AS, active surveillance; GPS, Genomic Prostate Score (Genomic Health, Redwood City, CA); MRI, magnetic resonance imaging.

within 6 months of diagnosis. It was not possible based on the CPT code and other EHRs to ascertain why the genomic test or MRI were ordered. Citing retrospective cohort data, guidelines have suggested that MRI may be useful to detect extracapsular extensions to aid in decision making for nerve-sparing surgery.<sup>2</sup> Although MRI has been considered an adjunct in risk assessment, the lower use of AS with MRI is consistent with the possibility that MRI is being used more for treatment staging rather than as a decision aid for AS use. The observation that approximately one in six patients underwent GPS testing and/or MRI may reveal an unmet need by physicians (and/or their patients) for more information beyond stage, Gleason score, and PSA value to aid in treatment decisions.

The use of AS varied widely with GPS and/or MRI testing and with age; in contrast, AS use did not vary based on geographic region, insurance status, or recorded information on presence of urologic symptoms or respiratory/chest diagnoses. AS use was approximately 43% for patients who underwent MRI, 60% for patients with no GPS or MRI testing, and 89% among patients with GPS testing only. Although published rates of AS use during the 2000s were low (<10%), recent studies have shown notably higher rates (40%-50%) with considerable variation between and among practices. The higher rates often are attributed to confidence in AS for patients with low-risk disease due to publication of the Prostate Intervention Versus Observation Trial (PIVOT) and the Prostate Testing for Cancer and Treatment (ProtecT) trial.<sup>26,27</sup> It is notable that the AS rates with no GPS or MRI testing observed in our study are consistent with rates recently reported by the MUSIC groups.<sup>5</sup> Despite the publication of large clinical trials, the level of AS



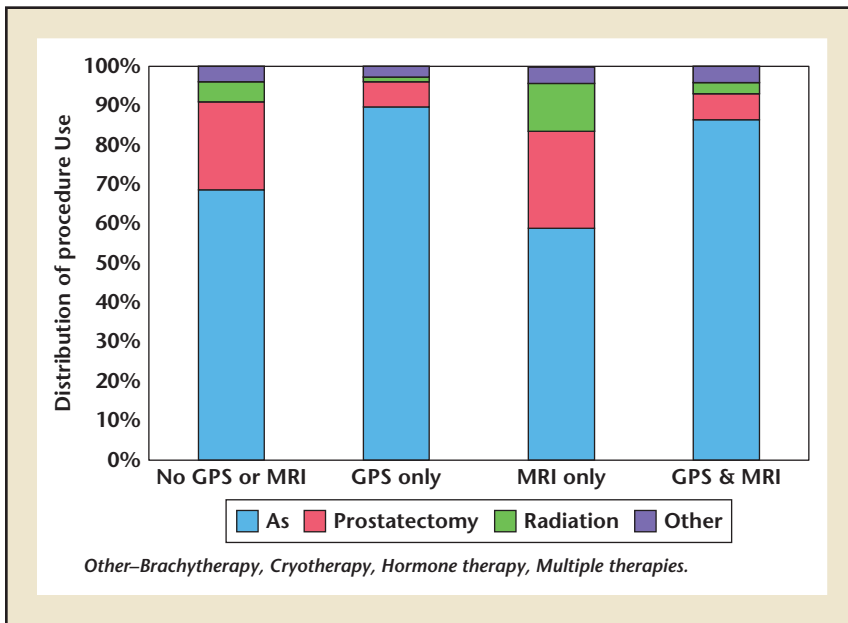


Figure 5. Distribution of procedures by GPS and/or MRI. GPS, Genomic Prostate Score (Genomic Health, Redwood City, CA); MRI, magnetic resonance imaging.

use in general remains below full adherence with preferred management recommendations published in guidelines.

6 and 12 months. Second, because no unique CPT code for AS exists, we defined it as no definitive therapy during the observation period.

**We found that 17% of patients with low-risk PCa underwent some evaluation with GPS testing or MRI within 6 months of diagnosis.**

Several limitations are inherent to a study design with an EHR and claims database. First, some patients followed to 6 months had no follow-up data at 12 months, which may be due to patients seeking care elsewhere, an insurance change, or a small risk of mortality between

This definition likely captured the majority of AS patients, but may have permitted some misclassification (some selected patients may not have truly undergone guideline-based AS). Finally, physicians who ordered the GPS test may have had different, unmeasurable,

perspectives toward adoption of emerging medical technologies compared with those who did not order the test and thus may not be representative of the field at large.

Clinicians, guideline panels, and insurers want answers to relevant questions when considering policies for the adoption of novel technologies such as genomic testing. For example, how does the intervention affect clinical management, especially among diverse patient populations seen in different clinical settings? Questions about real-world adoption and effects are well answered by collecting data in a broad range of settings. These results add to those from three such studies<sup>18-20</sup> of the Oncotype DX GPS assay and demonstrate consistent positive impact of the GPS test on AS use among different physicians and practices, geographic regions, and patients with different insurance coverage, over the >4 years that GPS has been commercially available.

## Conclusions

AS is a guideline-“preferred” intervention for low-risk PCa due to the avoidance of side effects of definitive therapy, detrimental effects on quality of life, and unnecessary treatment of small, indolent

**TABLE 4**

**Summary of Published Studies of Genomic Prostate Score (GPS) Testing and % Active Surveillance Use Among Men With American Urological Association Clinically Low-risk Disease.**

| Study   | Sample Size               |            | Active Surveillance, %        |                |                         |
|---|---------------------------|------------|-------------------------------|----------------|-------------------------|
|   | Baseline (Non-GPS Tested) | GPS Tested | Baseline (Non-GPS Tested) (%) | GPS Tested (%) | Absolute Difference (%) |
| Dall’Era MA et al. <sup>20</sup>                        | 68                        | 85         | 49                            | 76             | 27                      |
| Albala D et al. <sup>19</sup>                           | 71                        | 51         | 38                            | 59             | 21                      |
| Eure G et al. <sup>18</sup>                             | 167                       | 179        | 50                            | 79             | 29                      |
| Canfield S et al. <i>Rev Urol.</i> 2018 [current study] | 7746                      | 375        | 60                            | 89             | 29                      |

GPS, Genomic Health, Redwood City, CA.

cancer.<sup>2</sup> Combined with the results of other studies from multiple settings,<sup>18-20</sup> GPS testing is consistently associated with higher rates of AS compliance compared with MRI or no GPS/MRI testing at all. ■

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### MAIN POINTS

- Guidelines from the National Comprehensive Cancer Network and American Urological Association encourage active surveillance (AS) as a preferred management option for men with low-risk prostate cancer (PCa).
- Several studies reveal trends and variations in AS use among men seen in real-world settings. One analysis of 115,208 men diagnosed with clinically low-risk PCa found that 14,180 (12.3%) were initially managed by AS. Use of AS varied between 0% and 100%, with more than 58% of the variation associated with patient-level factors, such as age, race, stage, prostate-specific antigen level, and comorbidities. Approximately 10% of the variation in AS use was associated with nonmedical factors, such as treatment facility type or facility volume.
- We conducted a prospectively designed, retrospective assessment of electronic health records and administrative claims data to assess AS use for patients tested with a 17-gene Genomic Prostate Score™ (GPS; Genomic Health, Redwood City, CA) assay compared with those tested with only MRI and those not tested with genomics or MRI, during the same period of time.
- In a large US payer system, the GPS assay was associated with significantly higher AS use at 6 and 12 months compared with men who had MRI only, or no genomics and MRI testing. The higher AS utilization with GPS is aligned with guideline-based care.