original reports

Impact of a Genomic Test on Treatment Decision in a Predominantly African American Population With Favorable-Risk Prostate Cancer: A Randomized Trial

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abstract

PURPOSE The Genomic Prostate Score (GPS), performed on biopsy tissue, predicts adverse outcome in prostate cancer (PCa) and has shown promise for improving patient selection for active surveillance (AS). However, its impact on treatment choice in high-risk populations of African Americans is largely unknown and, in general, the effect of the GPS on this difficult decision has not been evaluated in randomized trials.

METHODS Two hundred men with National Comprehensive Cancer Network very low to low-intermediate PCa from three Chicago hospitals (70% Black, 16% college graduates) were randomly assigned at diagnosis to standard counseling with or without a 12-gene GPS assay. The primary end point was treatment choice at a second postdiagnosis visit. The proportion of patients choosing AS was compared, and multivariable modeling was used to estimate the effects of various factors on AS acceptance.

RESULTS AS acceptance was high overall, although marginally lower in the intervention group (77% *v* 88%; $P = .067$), and lower still when men with inadequate specimens were excluded ($P = .029$). Men with lower health literacy who received a GPS were seven-fold less likely to choose AS compared with controls, whereas no difference was seen in men with higher health literacy ($P_{interaction} = .022$). Among men with low-intermediate risk, 69% had GPS values consistent with unfavorable intermediate or high-risk cancer. AS choice was also independently associated with a family history of PCa and having health insurance.

CONCLUSION In contrast to other studies, the net effect of the GPS was to move patients away from AS, primarily among men with low health literacy. These findings have implications for our understanding of how prognostic molecular assays that generate probabilities of poor outcome can affect treatment decisions in diverse clinical populations.

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INTRODUCTION

Men with relatively low-risk prostate cancer (PCa) face a difficult choice between immediate therapy or active surveillance (AS) with possible deferred treatment. AS is now considered a safe alternative for properly selected patients. Although the adoption of AS in the United States has increased dramatically over the past few years, its adoption may be lagging among Black men.[1,2] There are persistent concerns about whether AS is equally safe in this high-risk group, because of differences in biologic aggressiveness of the cancers, reduced compliance with follow-up because of problems with access to care, and potential undersampling of tumors located in the anterior portion of the prostate.[3-8]

The Oncotype DX Genomic Prostate Score (GPS), performed on biopsy tissue, produces an outcome prediction using a model that accounts for the expression levels of 12 genes plus clinical features. Earlier studies demonstrated the added value of the GPS for predicting adverse pathology.[9,10] However, these independent validation studies were conducted in populations that are mainly White and relatively affluent. Furthermore, although such studies are critical for establishing that a new biomarker accurately predicts the targeted events, the ultimate clinical utility of such biomarkers, which are decision support tools, also depends on how they affect actual patient decisions. This is particularly important for biomarkers that provide physician and patient with probability information rather than discrete predicted outcomes.[11]

We conducted a randomized trial in a predominantly Black population from three public hospitals to determine the effects of adding the Oncotype assay to standardized National Comprehensive Cancer

ASSOCIATED CONTENT

Data Supplement
Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

Although active surveillance (AS) is now recommended for management of favorable-risk prostate cancer, patient selection remains a concern. The Genomic Prostate Score (GPS), a 12-gene assay performed on biopsies and validated for predicting adverse outcomes, is essentially a decision support tool. No studies to date have evaluated this assay's impact on treatment choice and decision quality among Black or lower socioeconomic status men. We conducted the first randomized trial comparing the GPS with standard counseling, enrolling AS-eligible patients from three public hospitals.

Knowledge Generated

AS adoption was high overall, but sharply lower with GPS among men with low health literacy. Positive family history and having insurance, but not race, were independently associated with choosing AS.

Relevance

Population characteristics should be accounted for when predicting the effects of a complex biomarker such as GPS. The net benefits may be weighted more toward avoidance rather than adoption of AS.

Network (NCCN)-based risk counseling. Here, we report the effects on treatment choice by the participants, the primary trial end point, as well as effects on decision conflict and regret. Previous observational studies, also conducted in populations with sparse representation by Black or low-income men, observed that the GPS increased adoption of AS.[12-14] We prespecified a hypothesis that this biomarker would increase adoption of AS among all patients, including Black men. However, this type of biomarker could also improve risk stratification, especially in high-risk populations, by detecting PCa that is aggressive despite reassuring standard clinical parameters.

METHODS

Study Design and Participants

The ENACT (Engaging Newly Diagnosed Men About Cancer Treatment Options) trial was conducted at three sites: the University of Illinois at Chicago, John H. Stroger Jr Hospital of Cook County, and the Jesse Brown VA Medical Center. Men with newly diagnosed PCa deemed eligible for AS were invited to enroll if age < 76 years, Eastern Cooperative Oncology Group 0-2, life expectancy > 10 years, and NCCN risk level favorable intermediate or below. Based on consensus among participating urologists regarding AS eligibility, the favorable intermediate definition was slightly modified from NCCN criteria to exclude cases with Grade Group 2 and > 3 positive cores and include patients with prostate-specific antigen (PSA) 10-20 ng/mL if PSA density was < 0.15. PSA density is a known predictor of biopsy reclassification on AS at first biopsy.[15] These modifications allowed only four unfavorable intermediate cases by NCCN to be eligible because of high prostate volume. Informed consent was obtained from all participants; the study Protocol (online only) was approved by committees for the protection of human subjects at all sites.

Participants received their diagnosis and identical counseling regarding treatment options at the first visit (V1) after diagnostic biopsy (Data Supplement, online only). At V1, they were randomly assigned to intervention or control, using a block random assignment scheme stratified on trial site and NCCN risk level. Baseline data on comorbidity, urinary and sexual function, health literacy, and psychologic indicators were obtained using standardized instruments (see the Data Supplement). Participants returned for a second visit (V2) within 2-3 weeks to discuss their GPS report (if so assigned), receive reinforced NCCN-based risk counseling, and make a treatment decision. A third visit (V3) was scheduled approximately four weeks after V2 but before treatment to collect follow-up surveys and determine if treatment choice had changed. A fourth study visit (V4) was conducted at the first clinical encounter after recovery from surgery, completion of radiation, or the first AS monitoring encounter. To assess perceived decision quality at V3, participants completed the 10-item Decisional Conflict Scale validated for men with relatively low health literacy who faced a decision about PCa screening.[16] At V4, participants completed a five-item decision regret questionnaire validated in cohorts of patients who had made decisions about cancer therapy, including PCa treatment.[17] Details concerning both decision quality instruments are provided in the Data Supplement.

Trial Interventions

Participating urologists agreed to offer three treatment options to each participant (surgery, external beam radiation, and AS) and to provide standardized counseling. They also agreed to personally complete all study visits with each participant to ensure communication from a single source. Standardized counseling emphasized the NCCN risk level, and the potential benefits and risks of each management option. Counseling for patients assigned to GPS included discussion of any GPS-related change in NCCN level, the GPS relative to others with the same baseline risk, and the adverse outcome probabilities. The GPS report format changed twice during the trial. Versions 1 and 2 contained only graphical differences; version 3

added estimates of the 10-year likelihood of metastasis and PCa death, based on a retrospective study of a surgical cohort.[18] One participant received version 1, 20 received version 2, and 70 received version 3. Study pathologists selected blocks containing the largest amount of tumor with the highest grade, and tissue sections or blocks were sent to Genomic Health, Inc for analysis.

Statistical Analysis

We used *t*-tests and chi-squares to assess balance after random assignment and explore the confounding structure within the data. In intention-to-treat analyses for the primary end point, treatment choice at V2, we used Fisher exact tests to compare assigned groups, in the whole population and within racial strata. We fit unadjusted logistic regression models, with and without two subjects who were undecided at V2, to compute odds ratios (ORs) and 95% CI for selection of AS versus immediate therapy. We also ran analyses excluding all GPS-assigned men who did not receive a GPS report, and others adding back those with tumors too small for the assay. The results from all three GPS report versions were combined since we found no differences in outcome. In stratified analyses, AS adoption was compared within subgroups using contingency tables and chi-squares. Multivariable logistic regression modeled the treatment choice of AS at V2. Multiplicative interactions between group and other covariates were tested to detect effect modifiers. Backward selections were performed for demographic and other variables, with significant effect modifications retained in the model. All statistical tests were two-sided, controlling for a .05 type I error probability. SAS version 9.4 (Cary, NC) was used for all analyses.

RESULTS

The Trial Population

A total of 1,315 consecutive patients with biopsies positive for cancer were screened and 317 (24%) were deemed eligible (Fig 1). Risk level above low intermediate was the dominant reason for ineligibility. Nine patients had insufficient tumor and one had excessive inflammation that prohibited performing the GPS assay. Seventy percent of the 200 participants were African American, 16% had a college degree, 46% were classified as having low health literacy, and only 12% had private insurance (Table 1).[19] Additional information on baseline characteristics is provided in the Data Supplement. Random assignment evenly balanced key variables at baseline, except for PCa in a first-degree relative and Sexual Health Inventory for Men score indicating severe erectile dysfunction, which were less common in the intervention group (Data Supplement) and thus were given particular attention as potential confounders in the analysis. Participating urologists, who had approximately equal numbers of patients assigned to each group, favored AS in 86% of cases immediately before the first visit after diagnosis.

Treatment Choice at Visit 2

Nine men dropped out after V1, leaving 191 evaluable for treatment choice at V2. In an intention-to-treat analysis (Table 2), assignment to GPS was associated with a marginally lower likelihood of choosing AS versus immediate therapy ($P = .067$). With exclusion of 10 men assigned to GPS who did not receive a result, the association was slightly stronger ($P = .029$). In unadjusted analyses, intervention decreased the relative odds of choosing AS by approximately 50%. Including or excluding two men who were undecided at V2 had no effect on the results.

The ultimate choice of management approach was closely linked to a change in the urologist's treatment preference after receiving the GPS result. After GPS, urologist preference changed from AS to treatment 18 times and only three times from treatment to AS. By contrast, urologist preference for controls went from AS to treatment only five times, and from treatment to AS only twice. The Decisional Conflict Scale, which ranges from 0 (lowest) to 40 (highest) and covers a participant's perception of preparedness and support as well as uncertainty, did not significantly differ between control and GPS groups; means (standard deviation) were 5.56 (7.25) and 4.60 (7.17), respectively, $P = .37$. Scores on the Decision Regret Scale, which ranges from 5 (lowest) to 25 (highest), also were not significantly different between control and GPS; means (standard deviation) were 7.54 (2.92) and 8.28 (3.38), respectively, $P = .12$.

Subgroup Analysis

As anticipated, GPS results varied widely within risk levels but there was a clear association between GPS and pre-test NCCN risk. In addition, immediate treatment was associated with higher GPS results within risk levels (Fig 2). The effects of GPS on treatment choice in various patient subgroups are shown in the Data Supplement. In a planned comparison, we found no significant differences in treatment effect based on race. The only variable that significantly altered the effect of the intervention was health literacy, which was prespecified as a potential effect modifier. Among men with below-median health literacy, the OR for AS comparing intervention with control was 0.16 (95% CI, 0.04 to 0.63), whereas the above-median OR was 1.12 (95% CI, 0.40 to 3.19).

Multivariable Model for Treatment Choice

In multivariable models, low intermediate status was a strong negative predictor for AS compared with very low-risk status, while low-risk status was also negatively associated (Table 3). Men with a positive family history of PCa had four-fold greater odds of choosing AS, and for those with any health insurance (including private or government-provided plans), AS was three times more likely. Among men with higher literacy, GPS had no significant effect. However, for men with lower health literacy, GPS was associated with seven-fold lower odds of choosing AS

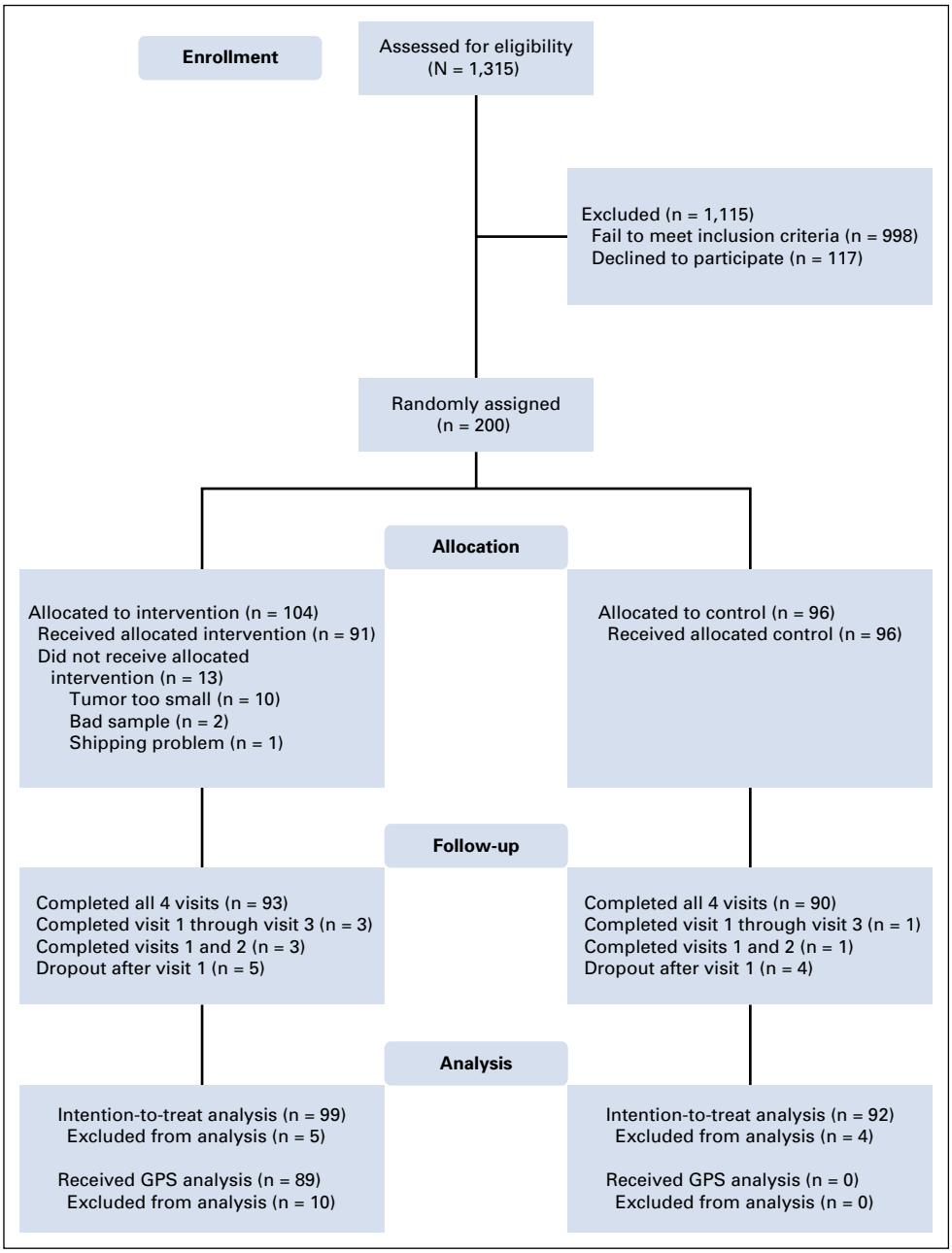

FIG 1. CONSORT diagram for the ENACT trial. ENACT, Engaging Newly Diagnosed Men About Cancer Treatment Options; GPS, Genomic Prostate Score.

($P_{interaction}$ = .022). No other variables showed significant independent associations. The predicted probabilities for choosing AS based on the model (Fig 3) illustrate the divergent direction of the GPS effect depending on health literacy, as well as the joint associations for NCCN risk level, family history, and insurance status.

Change in NCCN Risk After GPS

GPS reports highlight pre-test NCCN risk status compared with the post-test NCCN risk most compatible with each patient's clinical factors plus GPS. Although the intervention effect is independent of baseline risk, we observed a shift in NCCN risk following GPS testing in 60% of men in the intervention group. Thirty-eight men (43% of those receiving a GPS) moved to a higher NCCN risk group and among those, 15 (39%) chose treatment rather than AS (Fig 4A). Only 15 (17%) men moved to a lower risk level, yet two of those chose treatment. Among 26 men who were initially low intermediate, 18 (69%) moved to unfavorable intermediate or high risk and 14 (54%) chose treatment. All 29 intervention men who were baseline very low risk chose AS, although 10 (34%) had GPS results consistent with a

TABLE 1. ENACT Trial: Selected Characteristics of the Randomly Assigned Groups at Baseline[a]

Characteristic	Control (n = 96)	Intervention (n = 104)	Total (N = 200)	*P*
Age, years	63.5 (6.4)	63.8 (6.9)	63.6 (6.6)	.750
Race or ethnicity				
African American	65 (67.7%)	75 (72.1%)	140 (70.0%)	—
European American	16 (16.7%)	17 (16.4%)	33 (16.5%)	—
Hispanic or Latino	15 (15.6%)	10 (9.6%)	25 (12.5%)	—
Asian	0 (0%)	2 (1.9%)	2 (1.0%)	.371
Clinical site				
Jesse Brown VA	40 (41.7%)	43 (41.4%)	83 (41.5%)	—
University of Illinois at Chicago	17 (17.7%)	20 (19.2%)	37 (18.5%)	—
Stroger Cook County	39 (40.6%)	41 (39.4%)	80 (40.0%)	.960
Highest educational level				
Less than high school	20 (21.0%)	14 (13.5%)	34 (17.0%)	—
High school	26 (27.0%)	29 (27.9%)	55 (27.5%)	—
Some college	37 (38.5%)	43 (41.4%)	80 (40.0%)	—
Bachelor's degree or above	13 (13.5%)	18 (17.3%)	31 (15.5%)	.544
Self pay, uninsured	17 (17.7%)	15 (14.4%)	32 (16.0%)	.527
Health literacy[b]	8.3 (3.3)	8.9 (2.9)	8.6 (3.1)	.198
Living alone	37 (38.5%)	37 (35.6%)	74 (37.0%)	.664
Family history of PCa	30 (31.4%)	18 (17.3%)	48 (29%)	**.021**
NCCN risk level				
Very low	40 (41.7%)	40 (38.5%)	80 (40.0%)	—
Low	34 (35.4%)	36 (34.6%)	70 (35.0%)	—
Low intermediate[c]	22 (22.9%)	28 (26.9%)	50 (25.0%)	.817
PSA, ng/mL	5.98 (2.54)	5.98 (2.35)	5.98 (2.44)	.982
Gleason grade group				
GG1 (3 + 3)	82 (85.4%)	80 (76.9%)	162 (81.0%)	—
GG2 (3 + 4)	14 (14.6%)	24 (23.1%)	38 (19.0%)	.150
Charlson comorbidity index	2.9 (1.8)	3.0 (1.8)	3.0 (1.8)	.694
IPSS (urinary function)	9.9 (7.5)	9.4 (6.9)	9.7 (7.2)	.627
SHIM score (sexual function)	16.0 (7.1)	17.3 (5.6)	16.8 (6.4)	.175[d]
Urologist Rx preference				
Surgery	10 (10.4%)	15 (14.4%)	25 (12.5%)	—
Radiation	1 (1.1%)	1 (1.0%)	2 (1.0%)	—
AS[e]	85 (88.5%)	88 (84.6%)	173 (86.5%)	.760

NOTE. Bold indicates statistical significance.

Abbreviations: AS, active surveillance; ENACT, Engaging Newly Diagnosed Men About Cancer Treatment Options; GG, Gleason grade; IPSS, International Prostate Symptom Score; NCCN, National Comprehensive Cancer Network; PCa, prostate cancer; PSA, prostate-specific antigen; Rx, treatment; SD, standard deviation; SHIM, Sexual Health Inventory for Men.

[a]Mean (SD) and n (%) are presented for continuous and categorical variables, respectively.

[b]Short-form Behavioral Health Literacy Score (BHLS; range, 0-12; < 9 considered low literacy).

[c]Definition of low intermediate modified from NCCN favorable intermediate as specified in Methods.

[d]Analysis by categorical SHIM score showed more severe erectile dysfunction in controls.

[e]Preference ascertained before visit 1. AS includes watchful waiting (n = 1).

higher risk level. Figure 4B shows the likelihood of adverse pathology from the prediction model versus degree of change in NCCN risk. The trend toward treatment with both a high probability of unfavorable pathology and an increase in risk level is clear, but with obvious exceptions such as the two men who reclassified as high-risk but nevertheless decided for AS.

TABLE 2. Association of Random Assignment to Oncotype DX GPS Assay With Treatment Choice: Second Visit After Diagnosis (Primary Trial End Point)

Treatment Choice	Control No. (%)	Intervention No. (%)	*P*
All participants (N = 191)			
AS[a]	81 (88)	76 (77)	—
Surgery or radiation	11 (12)	21 (21)	—
Undecided	0 (0)	2 (2)	.067
Including only participants assigned to intervention who received a GPS result (n = 181)			
AS[b]	81 (88)	66 (74)	—
Surgery or radiation	11 (12)	21 (24)	—
Undecided	0 (0)	2 (2)	.029

Abbreviations: AS, active surveillance; GPS, Genomic Prostate Score; OR, odds ratio.
[a]OR for AS, OR_{AS} (95% CI) = 0.49 (0.22-1.09). Model excludes two participants undecided at the second postdiagnosis visit.
[b]Odds ratio for active surveillance, OR_{AS} (95% CI) = 0.43 (0.19-0.95). Model excludes two participants undecided at the second postdiagnosis visit.

Changes in Treatment Choice

Sixteen men (10 intervention and six control, $P = .32$) changed treatment choice after V2, either at V3 or later, resulting in a different actual treatment received (Data Supplement). Five men in each group changed from AS to undecided at V3 but eventually accepted surveillance. Long-term follow-up on AS is ongoing; however, among participants who underwent surgery as initial therapy, there were negligible differences in adverse pathology after prostatectomy. Two of eight (25%) controls had dominant Gleason pattern four or extraprostatic extension, compared with four of 15 (27%) intervention participants. Another two (25%) controls had organ-confined Gleason grade 1 compared with five (33%) GPS-assigned men. Among 10 men who had an increase in NCCN risk because of GPS and chose surgery, three had adverse pathology, and all three were classified as high-risk post-GPS.

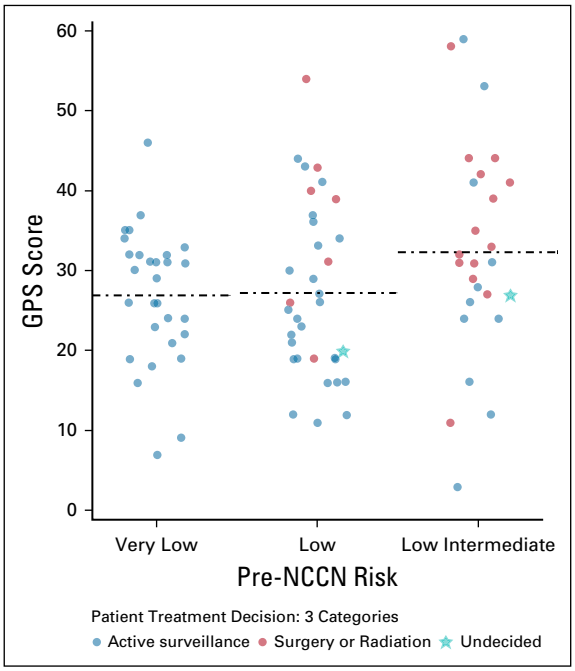

FIG 2. Relationship of GPS to treatment choice within NCCN risk level at baseline: intervention group only. Horizontal lines represent mean GPS: very low = 26.9, low = 27.2, low intermediate = 32.4. GPS, Genomic Prostate Score; NCCN, National Comprehensive Cancer Network.

TABLE 3. Multivariable Model for Predicting Patient Decision to Pursue AS at the Second Visit After Diagnosis (Primary Trial End Point)[a]

Variable	OR	95% CI
NCCN risk level		
Very low	1.00	Referent
Low	0.23	0.05 to 0.96
Low intermediate	0.03	0.01 to 0.12
Family history		
Negative	1.00	Referent
Positive	4.13	1.06 to 16.06
Insurance[b]		
Uninsured	1.00	Referent
Insured	3.16	1.00 to 9.92
High health literacy[c]		
Control arm	1.00	Referent
Intervention (GPS) arm	1.36	0.40 to 4.56
Low health literacy		
Control arm	6.52	1.30 to 32.73
Intervention (GPS) arm	0.88	0.25 to 3.10
	P interaction	.022

Abbreviations: AS, active surveillance; GPS, Genomic Prostate Score; NCCN, National Comprehensive Cancer Network; OR, odds ratio.
[a]Intention-to-treat cohort; n = 189.
[b]Insured includes Medicare or Medicaid and private insurance.
[c]High versus low health literacy defined as above or below median of Brief Health Literacy Screen.

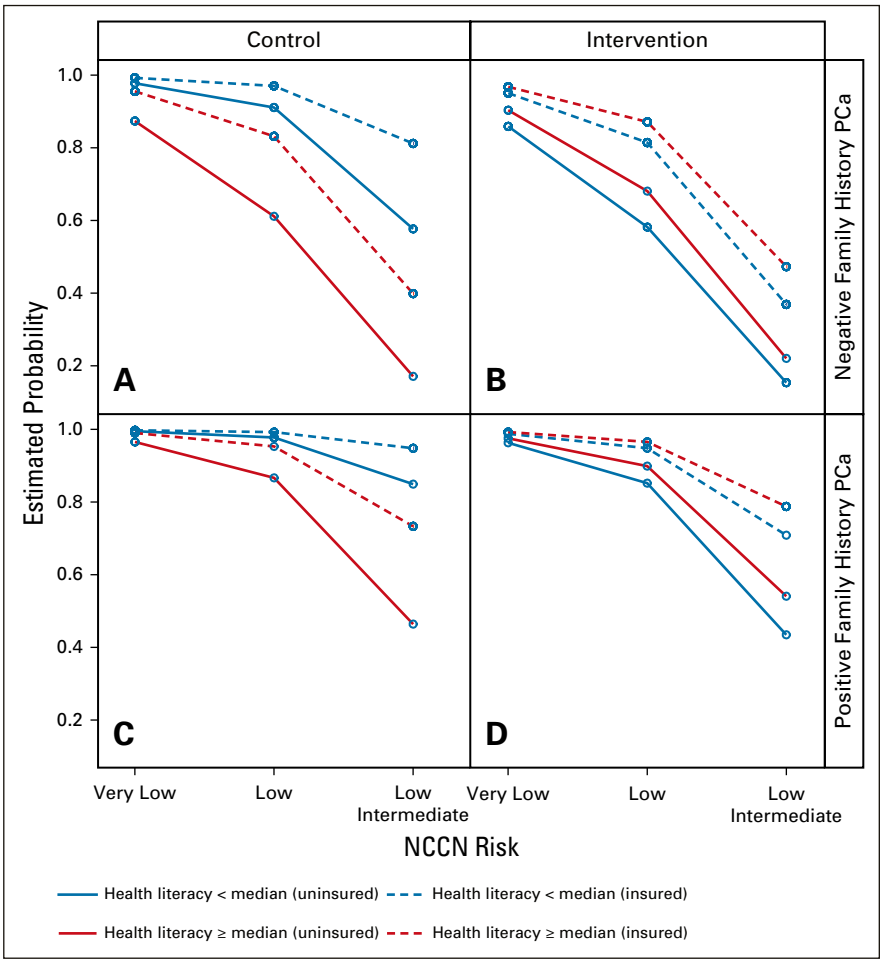

FIG 3. Predicted probabilities of choosing AS from the multivariable model showing all combinations of predictors, and modification of the Oncotype DX effect by health literacy. (A) Control group with negative family history of PCa. (B) Intervention group with negative family history of PCa. (C) Control group with positive family history of PCa. (D) Intervention group with positive family history of PCa. Note reversed positions for red and blue curves comparing control versus intervention groups (A *v* B and C *v* D). AS, active surveillance; NCCN, National Comprehensive Cancer Network; PCa, prostate cancer.

DISCUSSION

In this trial, acceptance of AS for management of relatively favorable-risk PCa was remarkably high, regardless of race, both among men who received the GPS prognostic assay and those who received only conventional risk counseling. Thus, we found that the GPS assay did not increase AS acceptance, and there was no apparent difference in its effect associated with race. Although the power to detect a significant increase in AS was limited by high baseline acceptance, we observed a marginally significant decrease in AS adoption among the GPS group, largely because of men with low intermediate risk who had GPS results consistent with a higher NCCN risk level. The GPS effect was highly dependent on health literacy, with essentially no effect among men with higher literacy, but much lower adoption of AS among men with low health literacy. Finally, the results were incompatible with a large GPS effect on perceived decision quality, as determined by decision conflict and regret surveys.

AS is now the preferred approach in national guidelines for management of favorable-risk PCa.[20,21] However, in 2015, only 36.4% of low-risk Black men in SEER received documented AS or watchful waiting versus 43.3% among comparable non-Black men.[22] In our trial, 80.7% of Black participants and 73.3% of non-Black participants ($P = .26$) chose AS, substantially higher rates than anticipated. These high rates of AS adoption, regardless of race, could be attributed to restricted inclusion of urologists who agreed to offer surveillance as a legitimate choice and counseling that emphasized unbiased discussion of treatments and a deliberate shared decision-making process.[23-25] Empirical evidence suggests that such a protocol can increase AS acceptance, and our data further indicate that this can be achieved in socially disadvantaged populations.[26-28] Our

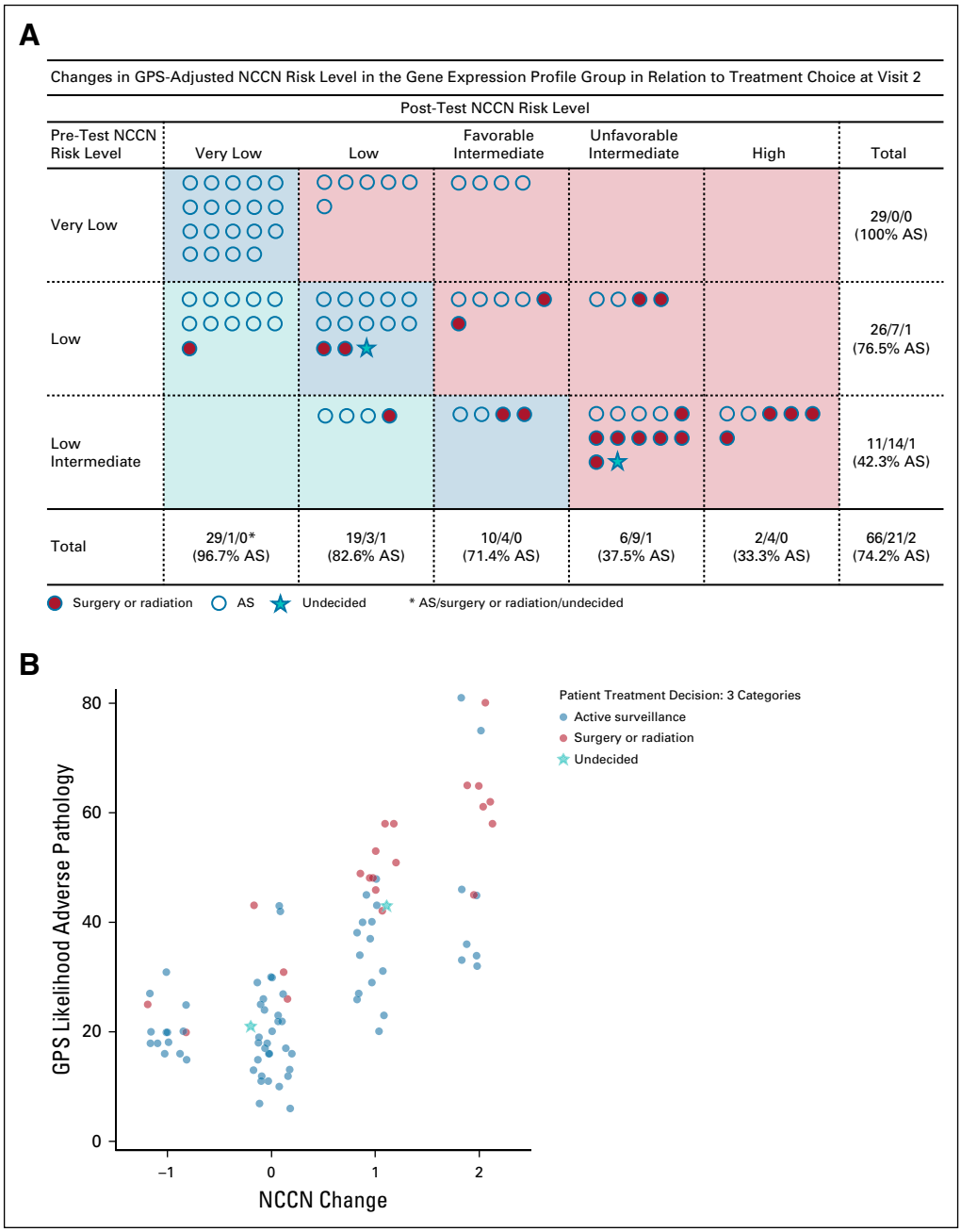

FIG 4. Effects of change in GPS-adjusted NCCN risk level on treatment choice from first postdiagnosis visit to the second in the group assigned to Oncotype DX (includes two patients who were undecided). (A) Table depicting treatment decision relative to pre- and post-test NCCN risk level; (B) magnitude of NCCN risk level change versus model estimated likelihood of adverse pathology at surgery. AS, active surveillance; GPS, Genomic Prostate Score; NCCN, National Comprehensive Cancer Network.

results showing concordance between urologist and patient regarding treatment choice, both initially and after GPS, supports the belief that urologist opinion has a strong effect on patient acceptance of AS.[29]

Nonexperimental studies in academic and community settings have reported that the GPS increases AS adoption.[12-14] In each study, adding GPS to clinical variables was associated with a net shift toward lower risk levels. In contrast, this randomized trial in a predominantly Black and lower socioeconomic scale population found an opposite net effect—that is, a shift toward higher risk levels and away from AS. Our data support the view that the GPS assay and similar prognostic biomarkers aimed at treatment choice are most useful in patients toward the upper end of the risk spectrum.[30,31] However, the movement away from AS is not simply explained by a higher prevalence of

intermediate risk at baseline, since intermediate risk prevalence (25%) in the trial was similar or even lower than in the observational studies. Among men with very low baseline risk, for whom the recommendation for AS is particularly strong, no GPS participants chose immediate therapy, whereas three control participants did. Thus, a larger study could confirm benefit from GPS at both ends of the risk spectrum.

By revealing tumor aggressiveness that is not apparent by clinical variables alone, the GPS may prove to be particularly useful in identifying men in this patient population with intermediate risk who should avoid AS.[32-34] Notably, mean GPS levels in ENACT were slightly higher within NCCN categories than previously reported in other studies.[9,35] Although the overall effect of the GPS on treatment choice was moderate, the strong effect among men with higher or lower health literacy was striking, suggesting that difficulty understanding the complex information involved may drive these patients toward immediate therapy. Although patients in the intervention group were slightly more likely to change their initial treatment choice, the data are too sparse to exclude an effect on decision stability.

The positive association we observed between family history of PCa and AS adoption was unanticipated. One study reported such an association, but this became nonsignificant after multivariable adjustment.[26] Further research should test the hypothesis that a positive family history is related to heightened awareness about PCa, including awareness of treatment-related morbidity and the rising acceptability of AS as a choice. Our observation regarding uninsured men is generally consistent with SEER data showing that observational management was less frequent in low socioeconomic status census tracts, and that men in these areas were less likely to defer treatment if they were uninsured or had Medicaid.[36] Uninsured men in our study had the option of receiving treatment without charge in a safety net hospital, whereas the prospect of indefinite care on AS could be perceived as daunting. In contrast to previous studies, being unmarried or living alone were not associated with treatment choice.[37]

This study benefitted from a randomized design, a homogeneous approach to risk counseling, and use of standardized survey instruments. However, several limitations and challenges should be noted. The number of participating urologists was restricted, partly to provide consistent counseling, and expanded participation could permit multilevel modeling of individual physician effects. We found no differences in the GPS effect despite changes in the report format. The 10-year probabilities for metastasis and death in the newer report were usually very low, even for men with high GPS results. Some men assigned to GPS failed to get a result because of insufficient tumor sample. These men were informed that their sample was too small to be assayed, which we considered to be a limited piece of potentially favorable risk information, and results both including and excluding this group were indistinguishable.

Although we found no main effect of GPS on decision conflict or regret, future analyses will explore psychometric variables in greater detail. Longer follow-up to assess treatment-related morbidity, AS adherence, and adverse reclassification, either after initial surgery or biopsy on AS, is ongoing. Given recent results on the predictive value of GPS assay for men on AS, it will be important to extend analyses to racially diverse AS cohorts with greater social disadvantage.[38,39] In addition, studies examining the effects of GPS combined with pre- or post-biopsy magnetic resonance imaging will be needed.[40] Finally, the cost-effectiveness of genomic testing is a concern, given the relatively high cost of the assay and the need to avoid overtesting patients who are least likely to benefit, such as those at extremely low risk.

In conclusion, we completed the first randomized trial, to our knowledge, of a prognostic multigene expression score on initial treatment choice among men with favorable-risk PCa. As more biomarkers yielding probability estimates enter the clinic, it is important to understand their impact on cancer treatment choice and decision quality in diverse patient populations. Any reasonable strategy for attacking the racial disparity in PCa outcomes should include AS, provided patients are judiciously selected for this option. However, this strategy must also emphasize improved early detection, as highlighted by the fact that nearly three quarters of the newly diagnosed men screened for this trial were ineligible because of an excessive NCCN risk level.

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CLINICAL TRIAL INFORMATION

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Impact of a Genomic Test on Treatment Decision in a Predominantly African American Population With Favorable-Risk Prostate Cancer: A Randomized Trial

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