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Patient and primary care clinician perspectives on polygenic risk scores for prostate cancer screening: a national qualitative study

Running title: Precision prostate cancer screening

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ABSTRACT

Purpose: Polygenic risk scores (PRS) have been proposed as adjuncts to clinical risk prediction for prostate cancer, but little is known about patient-centered implementation of PRS-informed shared decision-making (SDM). We explored patients' and primary care clinicians' perspectives on using PRS in SDM about prostate cancer screening.

Methods: We interviewed 2 national samples—male patients aged 40–60 years without prior prostate cancer, and primary care clinicians—within a national integrated healthcare system, about current screening practices, understanding of PRS, and anticipated impact on prostate-specific antigen (PSA) testing decisions. Transcripts were analyzed using a modified grounded theory approach.

Results: We interviewed 21 primary care providers (MD/DO/NP/PA), 7 primary care nurses (RN/LPN), and 42 patients. Many clinicians saw utility in PRS for individualizing screening, especially for high-risk patients, though some did not anticipate changing their PSA testing approach. Clinicians anticipated patients would struggle to understand PRS, and some patients did misunderstand genetic risk and how to interpret results. Most patients did not anticipate delaying or reducing PSA testing after low-risk results, but many said high-risk results would motivate earlier or more frequent screening.

Conclusion: Clinicians and patients anticipate acting on PRS results asymmetrically, favoring heightened screening for high-risk individuals but not reduced screening for those at low risk. Current PSA testing is already variable and not always guideline-concordant; introducing PRS will require additional strategies to promote high-quality SDM.

Keywords: Prostate cancer screening; polygenic risk scores; qualitative research

INTRODUCTION

Innovations in the acquisition, processing, and analysis of large-scale genomic data have the potential to usher in a new era of precision medicine, including risk-stratified approaches to prevention.[1,2] One such innovation is polygenic risk scores (PRS), cumulative estimates of genetic predisposition for certain diseases, such as type 2 diabetes or breast cancer.[3] By aggregating the effects of many genetic variants across an individual's genome, a PRS can stratify individuals by their likelihood of developing specific conditions, offering a potential tool for more personalized approaches to prevention and screening. Professional societies are actively deliberating how to include PRS in their clinical guidelines and position statements.[4–7]

Because of its high genetic heritability, prostate cancer is one disease for which a PRS performs particularly well in risk-stratifying individuals.[8,9] Men in the top 20th percentile of a prostate cancer PRS have twice the lifetime risk of developing prostate cancer,[8,9] and a recent large prospective screening study in the United Kingdom found that 22% of men aged 55 to 69 in the top 10th percentile of a PRS had clinically significant prostate cancer on a screening biopsy, defined as intermediate or higher risk by National Comprehensive Cancer Network criteria.[10] Many clinical prostate cancer PRS tests are already on the market, and several others are in development.[8]

Prostate cancer PRS tests thus represent an opportunity to improve approaches to prostate cancer screening, which is currently a thorny challenge for primary care due to conflicting clinical guidelines on whether and at what ages to recommend screening.[11–14] A PRS test might fill a gap recognized by the U.S. Preventive Services Task Force (USPSTF) and others, the need for better approaches for identifying men at

increased risk for prostate cancer to guide more tailored screening strategies.[11,15] That is, a prostate cancer PRS may help identify men at higher or lower risk, enabling a risk-adapted approach about whether, when, and how often to screen.[8] This tailored approach could reduce overdiagnosis and overtreatment among low-risk individuals while preserving the benefits of early detection for those at higher risk.[16]

At the same time, PRS will bring additional challenges to decision-making around prostate cancer screening. Current guidelines recommend shared decision-making about screening, a patient-centered process by which a patient and provider discuss different medical options and the risks, benefits, and patient value alignment of each.[17] Shared decision-making about prostate cancer screening is already complex, and the occurrence and quality of these conversations about prostate cancer screening are highly variable across healthcare settings in the U.S.[18–21] As PRS gain a greater clinical foothold, they may exacerbate the complexity and variability of high-quality shared decision-making. Understanding how patients and clinicians interpret and respond to this new unfamiliar laboratory test is thus critical to ensuring its appropriate and patient-centered use in shared decision-making. While PRS may offer a promising tool for tailoring prostate cancer screening, their integration into primary care raises important questions about communication, comprehension, and perceived clinical utility. Little is known about how patients perceive polygenic risk in the context of screening decisions or how clinicians might incorporate PRS into conversations that are already complex and preference-sensitive.[22,23] To address these gaps, we conducted a qualitative study of patients and primary care clinicians within a national integrated healthcare system to explore their perspectives on PRS for prostate cancer screening. Specifically, we

probed their understanding of PRS results of varying risk levels, the utility they perceived in the information, and the influence they anticipated that PRS results would have in their medical decision-making about prostate cancer screening.

METHODS

We conducted qualitative interviews with patients and primary care clinicians in a national integrated healthcare system. We sought to explore patients' decisional needs, including information, skills, and self-efficacy, for understanding and discussing PRS in the context of shared decision making about prostate cancer screening and to explore the needs, perceived competencies, and barriers faced by primary care providers and nurses in supporting patients in these decisions. The study was determined to be exempt by the VA Central IRB. Patient and clinician participants gave verbal informed consent.

Setting

The Veterans Health Administration (VHA) is the largest national integrated healthcare system in the U.S., caring for over 9 million military veterans.[24] Primary care in the VHA is delivered through a team-based model, wherein each Patient Aligned Care Team (PACT) typically includes one or more primary care provider, nurse care manager, clinical associate, and administrative clerk.[25] The VHA National Center for Health Promotion and Disease Prevention follows the USPSTF guidelines in recommending against universal prostate-specific antigen (PSA) testing for average-risk men, instead endorsing shared decision-making about the potential benefits and harms of screening.[11] However, screening practices vary widely across the VHA nationally.[26,27]

Patient recruitment and enrollment

We recruited a national sample of male VHA patient-participants aged 40–60 years without a personal history of prostate cancer or benign prostate disease. Eligible participants were identified through a query of the VHA Corporate Data Warehouse (CDW) using age and sex criteria, excluding individuals with relevant ICD-9, ICD-10, or CPT codes indicating a history of prostate cancer or related treatments. We used a purposive sampling algorithm designed to ensure representation of patients whose race was listed as African American/Black in the CDW, given the elevated risk of prostate cancer in this group, and variation in PSA testing history (approximately 50% with and 50% without prior PSA testing). This stratified random sampling was applied to a nationwide cohort of over one million individuals. An initial sample of 250 eligible patient-participants was selected and mailed recruitment letters, which included an opt-out postcard. Those who did not opt out within three weeks were contacted by study staff via telephone to confirm eligibility, provide study information, assess interest, and schedule interviews.

Primary care clinician recruitment and enrollment

We recruited a national sample of VHA primary care team members, including primary care providers [physicians (MD/DO), nurse practitioners (NP), physician assistants (PA)] and PACT nurses [registered nurses (RN) and licensed practical nurses (LPN)]. We included PACT nurses because in their role they apply VHA Clinical Preventive Services Guidance Statements to offer recommended screenings to patients, including cancers.[28] A random sample of 53 VHA facilities representing 15 states and territories was selected to reflect variation in U.S. region, rurality/urbanity, and the racial/ethnic

composition of local patient populations; site selection was facilitated using a large language model to generate a list of VHA sites varying by these criteria. The study team asked the Director of Primary Care at each selected site to disseminate a recruitment email to all eligible PACT members. Clinicians could express interest by clicking to send a prewritten reply email to the study staff, who then contacted interested clinicians to schedule interviews.

Theoretical models

Our approach to the patient and clinician participant interviews was informed by two complementary frameworks: the Ottawa Decision Support Framework (ODSF) and the Health Literate Care Model. The ODSF is a patient-centered model that identifies and addresses individuals' decisional needs—such as knowledge gaps, unclear values, or lack of support—to improve decision quality and alignment with personal values.[29] This framework guided our exploration of Veterans' and clinicians' informational, emotional, and practical needs related to shared decision-making about prostate cancer screening in the context of PRS. In parallel, the Health Literate Care Model emphasizes the creation of "productive interactions" between informed, activated patients and prepared, proactive care teams.[30] It highlights the importance of system-level supports, such as education and training for both patients and providers, to promote health literacy and engagement. This model informed our attention to communication strategies, role clarity, and the broader organizational context in which shared decision-making occurs. Together, these frameworks shaped the structure and content of our interview guides, which aimed to capture patient-, provider- and system-level factors influencing shared decision-making in precision cancer screening.

Data collection

We conducted one-on-one, semi-structured interviews with patient and primary care clinician participants using secure video conferencing technology (Microsoft Teams), each typically lasting 45–60 minutes. All interviews were conducted by two PhD-trained qualitative experts without clinical roles, to encourage more candid responses from both patient and clinician participants. Interviews were audio-recorded and professionally transcribed.

Prior to the interviews, patient and clinician participants were mailed and/or e-mailed a study information sheet describing PRS testing and three mock clinical reports indicating high (90th percentile), average (60th percentile), and low (10th percentile) polygenic risk for prostate cancer (Figure 1 and Supplementary Material).The mock clinical reports were developed iteratively by the study team, drawing on existing clinical PRS report formats[31,32] and reviewed by clinical and qualitative experts on the team for clarity, accuracy, and appropriateness for the target patient population.

Patient-participants were asked about their familiarity with and decision-making regarding prostate cancer screening and PSA testing, their understanding of genetic testing, and their willingness to undergo PRS testing. Interviewers then prompted patient-participants to think aloud as they read and interpreted the PRS information sheet and mock clinical reports. The interviewer gave participants the opportunity to ask questions about the report figures and gave further explanation, if requested. The interview used probing questions to explore their understanding of the reports, perceived meanings of the risk categories, and anticipated influence on future PSA

screening decisions. Demographic information was collected at the end of the interviews, including self-identified race and ethnicity.

Primary care clinician-participants were asked how they approach prostate cancer screening and their efforts at shared decision-making with patients about PSA testing. They were asked to look at the materials explaining PRS testing and to let the interviewer know if they had any questions or trouble understanding the materials. They were also asked how PRS screening might influence their approach to prostate cancer screening, including screening initiation, testing intervals for PSA testing, and patient communication.

Data analysis

Interview transcripts were analyzed using a modified grounded theory approach.[33–35] The core analysis team included a PhD-trained qualitative expert and two data analysts, and the larger study team included researchers with backgrounds in primary care medicine, genomics, health communication, and implementation science. An initial codebook was developed through a process of critical review and consensus building, drawing on both *a priori* concepts and impressions from early interviews. Codes were clearly defined to ensure consistent application across coders. Transcripts were coded using Atlas.ti 25 qualitative data analysis software. The team used iterative coding and memoing to capture emergent insights, with additional codes added as new themes arose from the data. The interdisciplinary composition of the analysis team supported diverse interpretive perspectives, while regular team meetings and memoing practices were used to surface and examine assumptions throughout the analytic process. Summaries of coded data facilitated the identification of thematic elements related to

knowledge of and decision-making about prostate cancer screening, clinical approaches to shared decision-making, understanding of polygenic risk and genetic testing, and the perceived impact of PRS on screening engagement.

RESULTS

Participant characteristics

Between May and November 2024, we interviewed 21 primary care provider-participants (MD/DO/NP/PA), 7 primary care nurses (RN/LPN), and 42 patient-participants. Forty percent of patient-participants were recorded as having Black or African American race, and 25% of patient-participants resided in rural areas of the U.S. (**Table 1**).

Themes

The analysis team identified several key themes from clinician and patient participants interviews related to the use of PRS in shared decision-making about prostate cancer screening.. While some clinician-participants were reluctant to make changes to how they approach PSA testing, many saw potential in the utility of the PRS test to guide individualized prostate cancer screening. However, clinician-participants anticipated that patients would have difficulty understanding PRS results and polygenic risk. Analysis suggested that some patient participants did indeed misunderstand the nature of polygenic risk and how to interpret the mock PRS results. Most patient-participants did not anticipate choosing to delay or reduce the frequency of PSA testing if they received low-risk PRS results. These themes are further discussed below (Figure 2).

Clinician perception of the clinical utility of PRS testing

Many clinician-participants thought the utility of the PRS test was in how they could provide individualized screening recommendations for their patients. They were open to the possibility of factoring the individual risk determined from the generic test into their approach to prostate cancer screening. Clinician-participants generally described this individualization as a modification of the frequency of screening instead of a decision whether to screen at all. One nurse said:

> *[I]f somebody is in the lower end maybe it's okay to do every two years for the PSA, if they are at high risk maybe every six months or more frequently to get the PSA done.* (RN, 90010)

Clinician-participants recognized a tension between clinical guidelines and the individualization that a PRS could afford in prostate cancer screening decisions, as illustrated by these two quotes:

> *I may not be that aggressive. Maybe I can screen him like every two years or something but I'm not going to be like, you know, oh, every year we need to get this done, you know? I mean that's me. I'm not sure it's our guidelines but that would make me comfortable doing every two years.* (MD, 90063)

> *[I]f the patient said, "You're the doctor. You decide," then I would order the PSA less likely or more likely depending on what the results show, going against the Task Force recommendations. I'd make it customized, in other words.* (MD, 90008)

Clinician discussions with patients about PRS results

Beyond the risk information conveyed by a PRS result, clinician-participants saw additional utility for PRS testing as a tool to prompt discussion with patients:

> *I think it definitely makes it easier to have a conversation should we even screen. Again, my experience is most people want screening. They [equate] that with good care.* (MD, 90023)

> *[T]he physician would have kind of more individualized backup to their discussions. Right now, the physicians will say, you know, "Most men of this age group have a risk," and "You have a family history," and it's all kind of up in the air and patients could have a tendency to kind of blow it off because, "That's not me. I don't have*

> *problems in that area." You know? "I don't need this screening. I don't want to hear about it." But, if you say, "You have these genetic markers which place you at this increased risk." Let's go ahead and have a discussion on how we can test for it, have a screening.* (RN, 90003)

However, one nurse participant observed that low-risk results might paradoxically lead to more challenging conversations with patients, compared with high-risk results:

> *I think it would make it easier for the people who are at an increased risk and more complicated for people that were at a decreased risk. Because if they think that they're at a decreased risk they might think, "Well, I don't need to get prostate cancer screening done."* (RN, 90058)

At the same time, some clinician-participants expressed concern that patients would overinterpret high-risk results:

> *I could see young men saying, oh, I have this marker, so I want a prostatectomy. And they're like 32 years old with no elevated PSA, nothing, which is not appropriate.* (MD, 90025)

Anticipated change to prostate cancer screening practices from PRS results

Despite the perception among some clinician-participants that PRS could help them provide more customized recommendations to patients, others reported that PRS results would not change their approach to PSA testing, citing routine practice recommendations and patterns:

> *No. I would probably do it when it's recommended.* (RN, 90058)

> *I don't think it would affect me. … I just lack the familiarity to put a lot of stock in only that and not checking PSAs, if that's what you mean.* (MD, 90023)

It was common for providers to order the PSA test reflexively as part of routine bloodwork, often prior to a patient's clinical visit so that the results could be reviewed during the visit. One physician stated, "*I think that that would leave my testing as it is. I tend to do a PSA test with all routine labs."* (MD, 90045)

Clinician perception of patient understanding of PRS

Clinician-participants anticipated that some patients would find it difficult to understand PRS results, due to low health literacy in certain patient groups and poor understanding of disease risk in the general population.

> *I think a patient like ours, who typically reads at the third grade level, is going to just throw it out. It's not going make any sense to them…I think when you start talking about a lot of probability, it becomes hard for our patients.* (MD, 90028)

> *[A]nytime you add statistics into what you're talking [about] with your patients, it's much more difficult. Yeah, I would think that it would make the conversation much more involved and actually less useful.* (MD, 90045)

Clinician-participants described this perceived lack of patient understanding as a significant barrier to engaging patients in discussions about PRS-guided prostate cancer screening.

Patient understanding of PRS results

Consistent with clinician-participant perceptions, we found some misunderstanding of probabilities among many patientparticipants. While some fully understood the information presented, communicating PRS results as percentiles led many to overestimate their risk, exemplified by this patient quote: "*I would consider it the same if I was in the 90th or in that 10%. Anything over zero*" (11215). Some patient-participants interpreted any percentile above 0% as an elevated risk warranting action. One stated: "I think even at 10% [10th percentile], I would be open to doing more" (10018).

Patient perception of genetic risk and modifiable risk

After viewing hypothetical high-risk PRS results, patient-participants generally anticipated they would be motivated to lower their risk through health behavior change, including screening and lifestyle modification. However, the language they used to

describe this motivation either conflated polygenic risk with modifiable risk or suggested they thought the report displayed a measure of their overall risk.

> *[A]t first I'd find out what the causes of it is, if it's something I'm doing, eating, or if it's hereditary, and then I would try, then I would start researching more about it to see what ways I can lessen those percentage down if there is a way.* (11152)

> *What can I do if I change my lifestyle? What would happen? Can it -- is there a way I can make it go down? Is a possibility through stress or through meditation and stuff, that I can do that to kind of calm my body down?* (10045)

> *I would ask my doctor, I mean, what I need to do to make sure that possibly can be reversed back to the lower risk level.* (10061)

At least one patient-participant anticipated attributing a high-risk PRS result to poor health behaviors:

> *I'd want to know what increased my odds or my chances? I'd want to know what I did wrong and what I can do right.* (11129)

Consistent with this misunderstanding, one patient-participant perceived value in rechecking the PRS after making lifestyle modifications:

> *Is there a way I can make it go down?…In six months, can I take another one to see if it's gone up?* (10045)

Patient anticipated behavioral response to PRS results by risk level

Patient-participants generally anticipated modifying their prostate cancer screening behaviors in response to risk results. Most agreed that a PRS result indicating higher risk of prostate cancer would warrant earlier or more frequent screening and that they would find such a result motivating to follow through with screening. One patient-participant captured the directionality of this correlation between risk and screening frequency:

> *65 percentile would be about, I say [PSA testing] every four months, four to five months, you know, and then at the 10% every eight months, at least every eight months, because within that timeframe…they can tell me, hey, you know, it went*

> *up a little bit. Let's see if we can, you know, put you on some medication. Let's see if we can just do a lifestyle change, you know, let's see what's going on with you…with the 95%, you know, every three months.* (10045)

In contrast, most patient-participants anticipated being hesitant to delay or reduce the frequency of screening if they received PRS results indicating low risk, as illustrated by one participant who stated: "[10th percentile] would make me feel a lot better, but I'd still want regular testing" (10067). One participant, when asked to explain his position on not reducing PSA testing if told he had a lower-than-average genetic risk, responded "I mean, what does that hurt? I'm already getting blood drawn for cholesterol and everything else in the world. So, why wouldn't I?" A few patient-participants suggested that low-risk results would lessen the urgency of prostate cancer screening, including the participant who stated:

> *I wouldn't have a real sense of urgency to, you know, "Oh. I really gotta get on this," you know? It'd be something that I would sort of kinda procrastinate with a little.* (11140)

In subgroup analysis by prior screening status, patient-participants who had previously undergone PSA testing were generally more likely to indicate that they would keep testing at the same or increased frequency, regardless of the hypothetical results of a PRS test. Participants who had not previously undergone PSA testing were generally similar, although some would be open to delaying initiating screening. No patient-participant, however, indicated that low-risk PRS results would cause them to forgo prostate cancer screening altogether.

Discussion

In this qualitative study of primary care clinician and patient participants within a national integrated healthcare system, we found that both groups recognized the potential value of PRS in guiding prostate cancer screening decisions but also identified substantial challenges to their effective use in practice. Clinicians expressed interest in using PRS to individualize screening frequency, but many were uncertain about how PRS would integrate with existing guidelines or influence their routine workflows. They also voiced concerns about patients' ability to understand polygenic risk information, particularly in populations with limited health literacy. These concerns were substantiated in patient interviews, where many participants misunderstood the meaning of PRS percentiles, conflated genetic risk with modifiable behaviors, or perceived PRS to a measure of overall risk. Although patients stated that hypothetical high-risk PRS results would motivate them to undergo prostate cancer screening earlier or more often, low-risk PRS results would not cause them to delay or reduce the frequency of screening. These responses may reflect a misunderstanding of quantitative risk, but they may also reflect patient-participants' underlying risk tolerance and value-based preference for vigilance in cancer screening.

Our findings reveal asymmetry in how both clinicians and patients interpreted and anticipated acting on PRS results: high-risk scores were seen as actionable and motivating, while low-risk scores were seen as a reassuring but not practice-changing. This pattern echoes prior research in cancer screening and risk communication, which has shown that individuals are more likely to respond to information that confirms the need for action than to information suggesting de-escalation of care.[36–38] In prostate cancer screening specifically, studies have documented patients' strong preferences for

continued PSA testing, even when informed of its limited benefit, and clinicians' tendency to default to routine screening practices.[38–41] In this study, the introduction of PRS appears to reinforce this dynamic, serving as a justification for more intensive screening when risk is high, but failing to reassure or shift behavior when risk is low. This risk asymmetry may reflect broader cognitive biases, such as loss aversion and action bias[36,42–44] and underscores the challenge of using polygenic risk information to support nuanced, preference-sensitive decisions. Without contextualization and targeted decision support, PRS may inadvertently amplify existing tendencies toward over-screening in the general population rather than promote more individualized care.

It is notable that, even in the absence of PRS, clinicians described significant variability in their existing prostate cancer screening practices. Many clinicians expressed deference to established guidelines but endorsed practice patterns, such as automatic PSA testing as a part of annual laboratory testing prior to an office visit, that are inconsistent with guideline-concordant shared decision-making. The introduction of PRS testing to prostate cancer screening will further complicate this landscape and likely exacerbate the variability in screening practice patterns, necessitating new implementation strategies to promote shared decision-making in preventive care. At the same time, it is worth noting that PRS could, under the right implementation conditions, strengthen the case for risk-stratified screening and support rather than undermine guideline adherence. For clinicians who currently apply PSA testing reflexively, a structured PRS-informed framework accompanied by clear clinical guidelines could provide a rationale for departing from one-size-fits-all testing and moving toward more individualized, evidence-based decisions. Realizing this potential will require the kind of

implementation science infrastructure including decision aids, clinician training, and guideline development that this study suggests is currently lacking.

These findings have important implications for the integration of PRS into routine primary care and prostate cancer screening. While PRS may offer a promising tool for risk stratification, their clinical use will require implementation strategies that promote understanding of the test results and how they affect the benefit-to-harm ratio of prostate cancer screening. Laboratories, clinicians, and health systems will need to communicate probabilistic polygenic risk in ways that promote patient understanding and informed decision-making, contextualized among other risk factors. Indeed, the potential confusion observed among patients about the meaning of polygenic risk may be partly attributable to the format in which PRS results were presented. The mock clinical reports used in this study conveyed PRS in isolation, without integration with other established risk factors such as age, family history, or genetic ancestry. Integrated risk models that combine PRS with clinical and demographic variables may communicate risk estimates that are more intuitively meaningful to patients and more actionable for clinicians. Integrated risk communication has been trialed for other diseases and cancer specifically,[45–47] and future implementation efforts should evaluate whether such integrated formats reduce misinterpretation and better support shared decision-making compared to PRS-only presentations.

As more is understood about the natural history of prostate cancer outcomes among men of varying PRS risk strata, clinical guidelines should be developed to help support clinicians and patients in shared decision-making. Without such supports, PRS may reinforce existing screening behaviors rather than promote more individualized,

values-concordant decisions. Specifically, clinical guidelines should state the degree of equipoise between the risks and benefits of screening for an individual at a given risk level. It is possible that high-risk individuals should receive a strong recommendation for screening, while the decision for individuals at average or low risk can be more preference-sensitive. Some have proposed a similar approach for lung cancer screening.[48,49] The appropriateness of adopting a similar approach for prostate cancer screening recommendations deserves further investigation.

While this study focused on prostate cancer, the findings may be more broadly applicable to the use of PRS in screening for other types of cancer, many of which are also clinically available or in development. A growing body of literature on PRS-informed cancer risk communication offers frameworks that may inform implementation efforts in prostate cancer screening.[46,50,51] For cancers such as colorectal, cervical, and breast cancer, where evidence for population-based screening is stronger, the introduction of PRS may interact differently with existing clinical workflows, patient expectations, and guideline structures than for cancers with less evidence for population-based screening, where preference-sensitive clinical conversations about personalized risk plays a more prominent role, such as prostate cancer and melanoma. Additionally complicating shared decision-making in cancer screening, some clinical tests offer PRS for dozens of diseases in one report.[32,45] The simultaneous receipt of multiple polygenic result types may impact patient decision-making around a single PRS result. How to optimize shared decision-making in the context of multiple polygenic results for a variety of diseases requires further study.

Strengths of this work include its theoretical grounding, the inclusion of both primary care clinician and patient perspectives, and the breadth of patients recruited across the U.S. This study also has limitations. First, as a qualitative study, the findings may not be generalizable to all patients or primary care clinicians, but they do provide in-depth insights into perceptions and decision-making processes. Second, participants responded to hypothetical PRS scenarios rather than their actual test results, which may not fully reflect real-world behaviors or emotional responses, both among patients receiving results and clinicians helping their patients make decisions with those results. Third, this study did not focus on several potentially important dimensions of PRS implementation, including the cost and accessibility of testing, patient and clinician trust in genetic testing (particularly among historically marginalized groups), privacy and data security concerns, and the feasibility of integrating PRS results into existing electronic health record workflows. These represent important areas for future research.

In conclusion, while PRS offer a promising avenue for personalizing prostate cancer screening, their successful integration into clinical practice will require more than just access to testing. Our findings suggest that both clinicians and patients are more likely to act on high-risk PRS results than to adjust behavior in response to low-risk findings, potentially reinforcing existing screening patterns rather than promoting individualized care. To realize the potential of PRS in supporting high-quality shared decision-making, implementation strategies must address gaps in understanding, communication challenges, and cognitive biases on both sides of the clinical encounter.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are not publicly available because they contain potentially identifiable qualitative interview data from research participants, but de-identified excerpts and additional study materials are available from the corresponding author on request and with appropriate approvals.

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AUTHOR CONTRIBUTIONS

Conceptualization: J.L.V., M.L.C.; Data curation: L.C., A.A.A.; Formal analysis: M.L.C., L.C., C.G.; Funding acquisition: J.L.V., M.L.C.; Investigation: M.L.C., C.G.; Methodology: M.L.C., J.L.V., C.G.; Project administration: A.A.A., L.C, V.S.; Resources: J.L.V., M.L.C.; Supervision: J.L.V., M.L.C.; Validation: M.L.C., L.C., C.G.; Visualization: C.A.B., J.L.V.; Writing-original draft: J.L.V., C.G., M.L.C.; Writing-review & editing: M.L.C., L.C., C.G., A.A.A., E.A., M.E.D., C.A.B., V.S., C.E.G., M.T.S., R.S.W., J.L.V.

ETHICS DECLARATION

This study was reviewed by the Veterans Health Administration Central Institutional Review Board and determined to be exempt human subjects research under exemption categories 2(ii) and 2(iii), with limited IRB review. Informed consent was waived in accordance with institutional and federal regulations.

Clinical trial registration: Not applicable.

CONFLICT OF INTEREST DISCLOSURES

The authors declare that they have no conflicts of interest.

ADDITIONAL INFORMATION

Supplementary Material: A combined PDF of supplementary figures, tables, and text, including the full PRS information sheet and interview guides, is submitted as a separate file.

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FIGURE LEGENDS

Figure 1: Images shown to patient-participants (Panels A-C) and primary care clinician-participants (Panels A-D) during interviews about polygenic risk score-informed prostate

cancer screening. See Supplementary Material for full materials and accompanying interview guides.

Figure 2: Key themes on polygenic risk scores for prostate cancer screening from interviews with primary care clinicians and patients.

Table 1. Characteristics of patient and primary care clinician participants interviewed about their perspectives on polygenic risk scores for prostate cancer screening.

	Patient-participants (n=42)	Primary care clinician-participants (n=28)
U.S. Region, n (%)		
Northeast	6 (14%)	1 (4%)
Midwest	8 (19%)	7 (25%)
South	20 (48%)	10 (36%)
West	8 (19%)	10 (36%)
Rurality Status		
Urban	32	--
Rural	7	--
Highly Rural	1	--
Missing	2	--
Age, mean (SD) years	51.8 (6.1)	--
Race, n (%)		
American Indian or Alaska Native	2 (5%)	--
Asian	2 (5%)	--
Black or African American	17 (40%)	--
Native Hawaiian or Other Pacific Islander	2 (5%)	--
White	19 (45%)	--
Ethnicity		
Hispanic/Latino	3 (7%)	--
Not Hispanic/Latino	39 (93%)	--
Clinician Type, n (%)		
Primary Care Provider (MD, DO, NP, PA)	--	21 (75%)
Nurse (RN, LPN)	--	7 (25%)

Percentages may not sum to 100% due to rounding. Abbreviations: DO, Doctor of Osteopathic Medicine; LPN, Licensed Practical Nurse; MD, Doctor of Medicine; NP, Nurse Practitioner; PA, Physician Assistant; RN, Registered Nurse; SD, standard deviation.

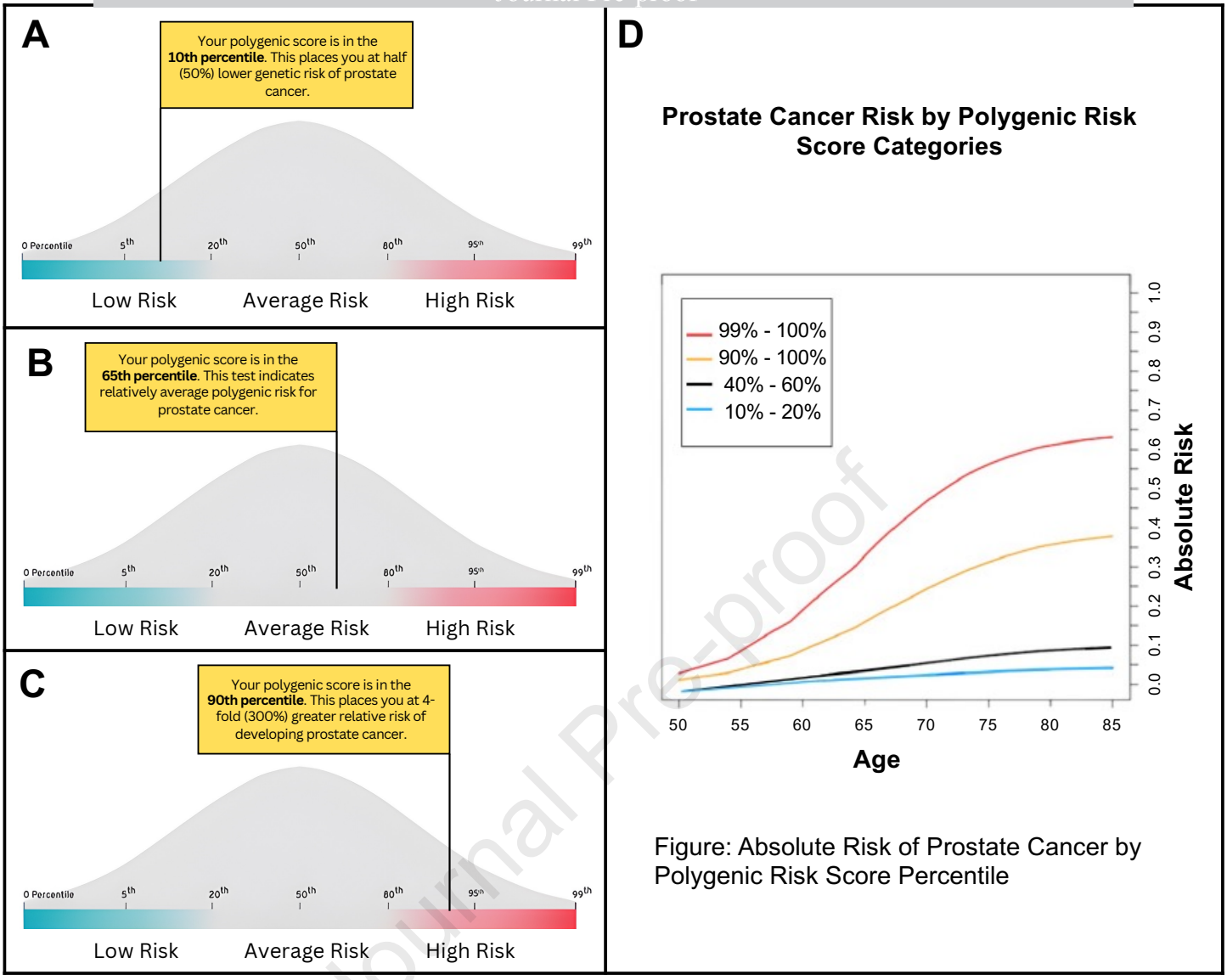

Figure: Absolute Risk of Prostate Cancer by Polygenic Risk Score Percentile

CLINICIAN PERSPECTIVES (n = 28)

1. **Perceived utility for individualized screening**
   Many clinicians saw PRS as a tool to tailor PSA testing frequency, particularly intensifying screening for high-risk patients.
2. **PRS as a prompt for shared decision-making**
   Clinicians described PRS as concrete, individualized tool that could open or strengthen conversations about prostate cancer screening.
3. **Concern about patient understanding**
   Clinicians anticipated that low health literacy and the probabilistic framing of PRS would make results difficult for many patients to interpret.
4. **Inertia of routine PSA testing practices**
   Some clinicians said PRS would not change their approach, citing reflexive PSA ordering with routine labs and adherence to existing recommendations.

PATIENT PERSPECTIVES (n = 42)

1. **Misinterpretation of probabilities and percentiles**
   Some patients treated any non-zero percentile as elevated risk, conflating PRS percentiles with absolute risk of prostate cancer.
2. **Conflation of genetic risk with modifiable risk**
   After viewing high-risk results, patients frequently described intentions to lower the score through diet, stress reduction, or lifestyle change.
3. **High-risk results motivate earlier / more screening**
   Patients overwhelmingly anticipated that a high-risk PRS would drive them to start PSA screening sooner or test more frequently.
4. **Low-risk results would not reduce screening**
   Few patients said a low-risk PRS would lead them to delay or space out PSA testing; most preferred to continue at current cadence.

CROSS-CUTTING FINDING

Asymmetric anticipated response to PRS results

HIGH-RISK PRS	→ Both clinicians and patients anticipated earlier or more frequent PSA screening
LOW-RISK PRS	= Neither group anticipated meaningfully delaying or de-escalating PSA screening