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**ARTICLE**

# *Understanding the utilization of genetic counseling and testing among patients with prostate cancer*

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***Objectives:*** *Prostate cancer (PCa) progression is influenced by a myriad of germline and/or somatic variants estimated to occur in 4.6%–11.8% of patients. Identified pathogenic variants may carry implications for treatment selection and prognosis. Despite the importance of genetic testing, referrals to counselling remain underutilized by urologists. This study aimed to understand referral patterns, testing uptake, and genetic results among men with PCa at a single large academic center.*

***Methods:*** *Records from 2010 to 2022 at Emory University were reviewed to identify men undergoing prostate biopsy and subsequent genetic counselling (CPT 96040). Referrals were confirmed as PCa-related and assessed against contemporaneous National Comprehensive Cancer Network (NCCN) criteria. Referral origin, genetic testing completion rates, and results were collected. Descriptive statistics summarized relevant results.*

***Results:*** *Of the 6995 prostate biopsies performed over the study period, only 70 of these patients saw a genetic counselor, of whom 49/70 (70%) were referred for PCa between 2010 and 2022, all meeting contemporary criteria for testing. Indications included high-risk disease (36.7%), metastatic disease at presentation (20.4%), and family history/ancestry (42.9%). Referrals increased from 0 prior to 2015 to 12 in 2022. Most originated from medical oncology (44.9%) or self-referral (12.2%), with urologists accounting for only 6.1%. Of those referred, 45 (91.8%) underwent genetic testing; 62.2% had negative results, 24.4% variants of unknown significance (VUS), and 4.4% tested positive for PCa-related pathogenic variants.*

***Conclusions:*** *Although referrals increased over time with guideline evolution, urologists accounted for a minority of referrals. While most results were negative or uncertain, pathogenic variants likely carried therapeutic significance. Addressing barriers to referral and improving integration of genetic services into urologic practice may help improve PCa care.*

**Key Words:** prostate cancer, genetic evaluation, genetic testing, referrals, variants

## Introduction

Prostate cancer (PCa) remains the most diagnosed malignancy worldwide, representing the 6th most common cause of cancer-related deaths in men.[1] Presenting mostly insidiously, a diagnosis of PCa is typically based on a complex combination of laboratory tests (such as prostate specific antigen; PSA), imaging tests (transrectal ultrasonography and multi-parametric magnetic resonance imaging) and image-guided biopsies.[1,2] Importantly, newer diagnostic modalities have emerged including free (vs. total) PSA, prostate-cancer-antigen 3 (PCA3) urine testing, prostate health index scoring (PHI), the "4K" test, prostate imaging-reporting and data system

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(PIRADs), and genetic testing while prior modalities continue to be reassessed.[1,3] With an estimated more-than one million cases diagnosed yearly worldwide, efforts aimed at understanding the key pathologic underpinnings of this malignancy continue to grow.[1] Although the exact cause of PCa has not been established, several key risk factors have been documented thus far, each with their own characteristics.[1] Previously noted risk factors have included increasing age, black/Afro-Caribbean ethnicity, obesity, and a family history positive for PCa.[1,4] Given the aforementioned associations observed between family history and risk of PCa development, as well as documented associations with certain hereditary cancer syndromes (i.e., Hereditary Non-polyposis colorectal cancer tumor spectrum; Lynch syndrome), increasing attention is being given to understanding the specific genetic underpinnings of this morbid disease.

Specifically, the pathogenesis and progression of PCa has been associated with various germline and somatic tumor genetic variants, such as the Breast CAncer gene 2 (*BRCA2)*, Ataxia-Telangiectasia Mutated (*ATM*), and MutS Homolog 2 (*MSH2*-implicated in Lynch syndrome) to-date.[5–8] Specific pathogenic/likely pathogenic variants (P/LPVs) are estimated to occur in 4.6% of patients with localized and 11.8% with metastatic disease, reflecting the increased genetic associations observed with tumor aggressiveness.[5,7] A recent study by Rodgers-Fouché et al. documented significant increases in PCa risk (15% incidence) among 235 male patients over a 24-year period, with more than half of such patients demonstrating a second primary cancer diagnosis.[9] Given the aforementioned genetic links, current clinical guidance recommends genetic evaluation for men with PCa and any of the following: (1) high-risk, very high-risk, regional, or metastatic PCa, (2) a personal history of a high-risk germline variant-associated malignancy (such as those part of the Lynch syndrome spectrum like colon and pancreatic carcinomas), (3) a strong family history of malignancy, or (4) high-risk ancestry (such as patients with Ashkenazi ancestry).[10]

Despite their clinical value, germline genetic testing and counseling by urologists in the outpatient clinical setting presents numerous challenges, including pre- and post-test counseling, selection of the appropriate test, and maintaining awareness of continuously rapidly-evolving clinical guidelines.[11,12] While referrals to genetic counseling services may offer means of navigating the complexities of genetic testing for patients, such referrals are often under-utilized by urologists.[13] A prior study by Loeb et al. demonstrated that only 55% of urologists reported access to a genetic counselor, and 25% of providers lacked knowledge on correct test selection.[13] Furthermore, this same study demonstrated that patients of younger age, those presenting to an academic practice, and patients presenting to urologists specializing in PCa/oncology had statistically significant increased odds of receiving germline testing.[12]

Thus, the use of genetic testing among urologists is likely multifactorial and limited by factors such as understanding and access, with genetic testing results likely carrying treatment and prognostic significance for such patients.[14–16] Given that genetic testing and counselling are critical for the diagnosis and management of PCa holding significant therapeutic implications (particularly in metastatic castrate-resistant disease) and for facilitating cascade testing among at-risk family members, further data analyzing referral practices and results is crucial.[10] As such, this study aims to critically assess referral patterns to genetic counseling, subsequent utilization of testing referrals, and test results among men with PCa that qualify for genetic evaluation based on National Comprehensive Cancer Network (NCCN) guidelines.

## Methods

### *Study design*

As this study was conducted using data retrieved from a quality improvement initiative, institutional review board (IRB) approval was not required, and informed consent was waived. Records at Emory University were reviewed to include patients undergoing prostate biopsy between 2010 and 2022. This period was chosen to reflect the evolution of genetic testing guidance and continued integration into clinical practice.[17–19] Prostate biopsy receipt was then selected as our initial inclusion criterion to maximize capture of patients who were seen by a urologist and eligible for genetic evaluation based on pathology results or clinical history. From the patients who underwent biopsy, those attending genetic counselling appointments were identified by CPT (current procedural terminology) code 96040 ("Medical genetics and genetic counseling services, every 30 min"), resulting in a cohort of patients with records indicating both a prostate biopsy and a genetic counseling appointment. Of note, this is the default code for genetic counseling appointments in our institution; additional CPT codes for 15-, 45-, or 60-min (or any other length) appointments do not exist.

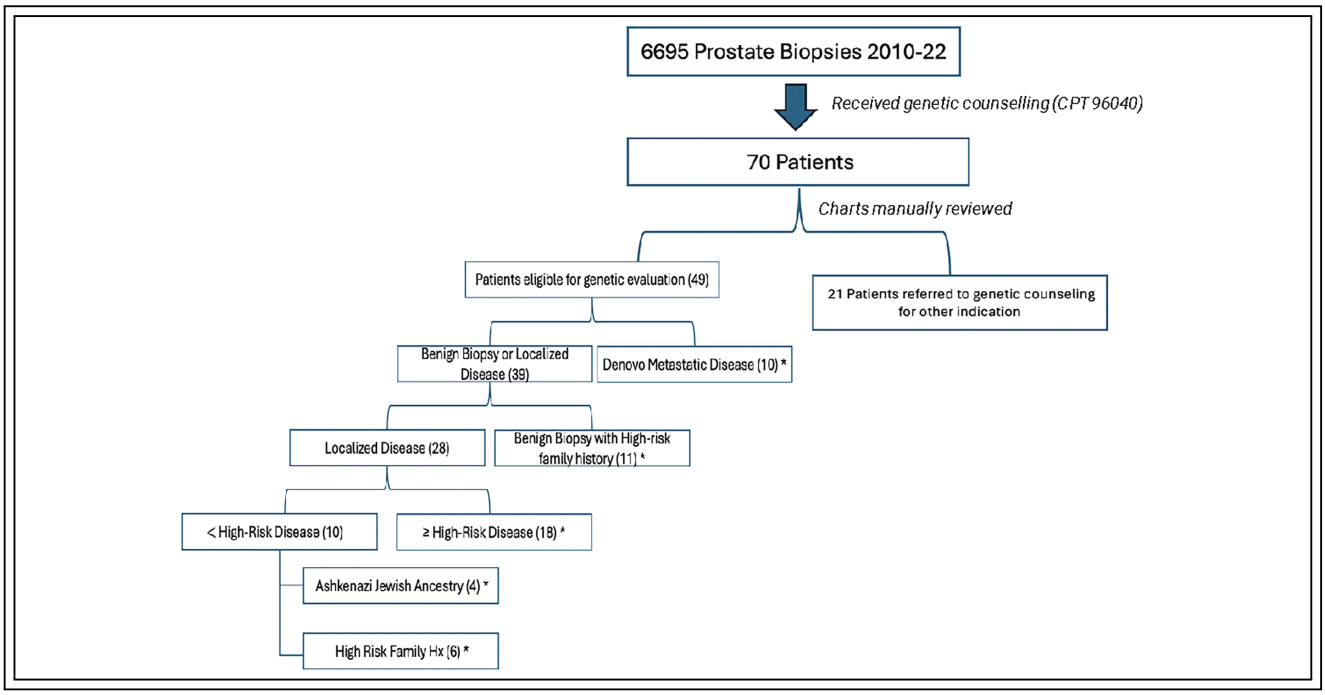


**FIGURE 1.** Flow diagram depicting patient population identification and indications for testing among those referred. Note. *Criteria for genetic testing referral, depicting how all referrals were done appropriately.

### *Data collection and analysis*

Following initial selection, a comprehensive review of electronic health records, for the subset of patients that underwent biopsy as well as genetic counseling, was conducted to remove any patients with negative biopsy results, ensure genetic counseling referrals were made specifically for PCa, and to evaluate whether they met referral criteria to genetic counseling during the period that a urologist was involved in their care using available guidance at that time.[10,20] High-risk features were defined as prostate-specific antigen (PSA) > 20 ng/mL, clinical stage T3 (cT3), or pathologic stage T3 (pT3) per clinical guidance (Figure 1).[10,20] The urology care period was defined as the time between their first urology clinic appointment for elevated PSA and/or prostate biopsy and their last note from a urologist with a main clinical complaint of elevated PSA or PCa. Indications for genetic counseling were based on current NCCN guidelines for the year that the prostate biopsy occurred. For those deemed appropriate for genetic evaluation, additional analysis was conducted to assess rates of genetic testing, P/LPV prevalence, and specific details regarding referral origins for genetic counseling. Genetic tests, dictated by genetic counselors, were performed using Invitae (San Francisco, CA, USA), Ambry Genetics (Aliso Viejo, CA, USA), and Myriad Genetics (Salt Lake City, UT, USA). Genes were determined as linked to the development of PCa through a combination of manual chart review of genetic test results, counselling notes, and subsequent confirmation using contemporary literature. Descriptive statistics, figure creation, and R-squared calculations were performed using Microsoft Excel (version 2512, Redmond, WA, USA) which summarized referral patterns, testing subtypes, and respective results.

## Results

There were a total of 6995 prostate biopsies performed over the study period between 2010 and 2022. We identified a total of 70 patients who underwent both prostate biopsy and genetic counselling, 49 (70%) of whom were referred during our study period. All these referrals were deemed to have been indicated based on NCCN guidance available at the time of referral. Common indications for genetic testing included (but were not limited to) the presence of very high or high-risk disease (18, 36.7%) patients, *de novo* metastatic disease (10, 20.4%), and a high-risk family history/ancestry (21, 42.9%); no patients met criteria based on high-risk pathology alone. Figure 1

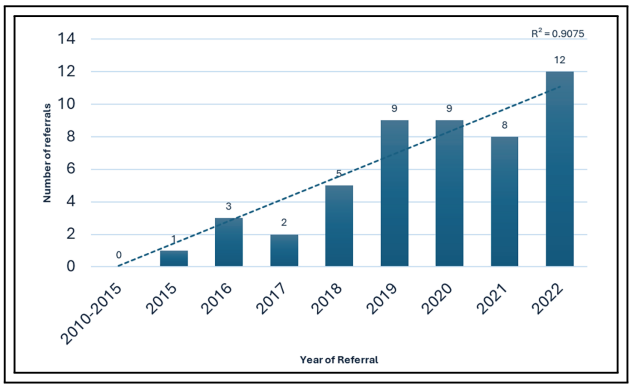


**FIGURE 2.** Increasing trend of genetic counseling referrals by all specialties over the study period

outlines the patient selection process and their respective indications for referral to genetic testing services. An increasing trend in the number of referrals was also observed from a total of 0 prior to 2015 to 12 referrals in 2022, depicted in Figure 2.

Referring specialty, type of genetic test received, and respective test results are detailed in Table 1. The majority of patients were referred by medical oncologists (22; 45%), followed by self-referrals (6; 12%), with only a minority of patients (3; 6%) referred by urologists (Figure 3). Of the 49 patients referred, 45 (92%) subsequently underwent genetic testing, with the majority having either negative results (28; 62%) or a variant of uncertain significance (VUS) (11; 24%) (Figure 3). The remaining 6 (14%) patients were found to carry genetic P/LPVs, 2 (4.4%) of which have been causally linked with the development of PCa.[1,3] Specific genetic tests, labs, and testing results alongside corresponding PSA and Gleason group scores are depicted in Table A1.

TABLE 1. **Referring to medical specialties, the type of testing received and results**[5,7]

| Covariate | Total (%) |
|---|---|
| **Referring specialty (N = 49)** | |
| Medical Oncology | 22 (44.9%) |
| Self-referral | 6 (12.2%) |
| Internal Medicine | 6 (12.2%) |
| Radiation Oncology | 4 (8.2%) |
| Dermatology | 3 (6.1%) |
| Urology | 3 (6.1%) |
| Gastroenterology | 2 (4.1%) |
| Neurology | 1 (2.0%) |
| Cardiology | 1 (2.0%) |
| Surgical Oncology | 1 (2.0%) |
| **Type of test received (N = 45)** | |
| Single gene testing | 3 (6.7%) |
| Multigene testing | 42 (93.3%) |
| Whole genome testing | 0 (0%) |
| **Genetic testing results (N = 45)** | |
| Negative | 28 (62.2%) |
| VUS | 11 (24.4%) |
| *FH* variant | 2 (4.4%) |
| *MSH2* variant* | 1 (2.2%) |
| *BARD1* variant | 1 (2.2%) |
| *BRCA2* variant* | 1 (2.2%) |
| *SDHD* variant | 1 (2.2%) |

Note. *Variants associated with prostate cancer development. Abbreviations: N, Number; VUS, Variant of unknown significance; FH, Fumarate hydratase; MSH2, MutS Homolog 2; BARD1, BRCA1-associated RING domain 1; BRCA2, BReast CAncer gene 2; SDHD, Succinate dehydrogenase complex subunit D.

## Discussion

In this study, several interesting findings were noted. First, a rapidly increasing trend in referrals between 2010 and 2022 was observed, likely reflecting continuous guideline evolution and increasing awareness by medical professionals at our institution.[10,20] Second, only a minority (6%) of referrals were made by urologists, with the rest of the patients being referred by medical oncologists or self-referring. Finally, despite only a minority of tests revealing pathogenic variants with known significance, almost a quarter of patients carried a VUS aligning with prior literature documenting a prevalence of 27%.[5,7,21] Importantly, of the 49 patients referred, 4 (8%) did not undergo subsequent genetic evaluation, the reason for which remains unclear.

The rising number of referrals to genetic services over the past decade observed in our results aligns with the maturation of clinical guidance.[18,19] In 2016, the first genetic evaluation guidelines for PCa were outlined by the NCCN, suggesting "consideration" of evaluation solely for patients presenting with PCa and a strong family history of BRCA 1/2 related malignancies, a consideration that quickly became redundant given the rapid increase in evidence.[19] In 2018, the guidance was further expanded to include those with metastatic and/or advanced disease and/or high-risk disease, and the "consideration" shifted to a "recommendation".[17–19] The increase in referrals correlating with clearer and expanding guidance likely reflects improvements in understanding

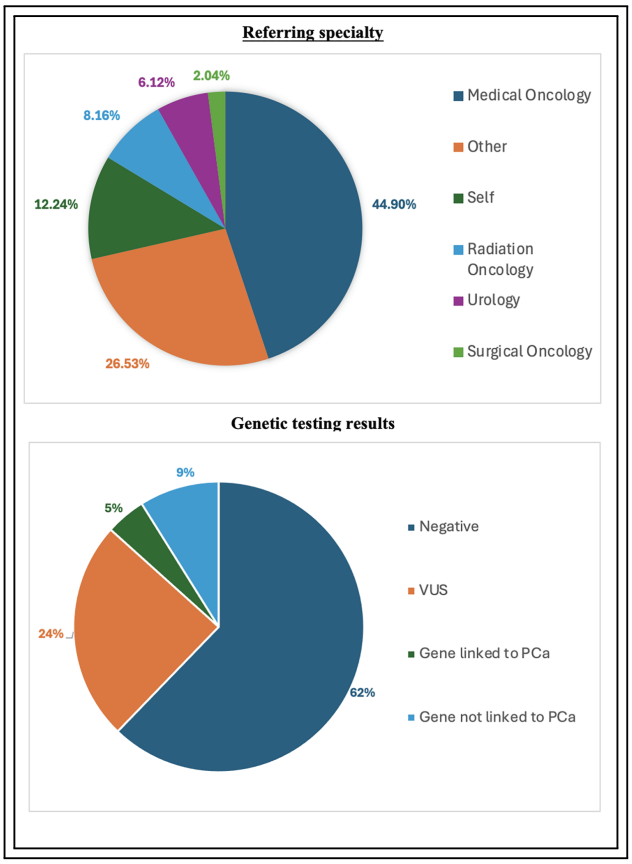


**FIGURE 3.** Referring subspecialties and genetic testing results.[5,7] Abbreviations: VUS, Variant of unknown significance; PCa, Prostate cancer

as well as awareness of genetic counseling services and their role may promote subsequent utilization, aligning with prior literature.[12,21] A prior study by Byrne et al. completed in the United States documented a drastic increase in the number of patients referred for genetic counselling between 2016–18 (2% of patients) and 2019–2022 (14%) attributed to increasing awareness through institution-led initiatives.[21] In their study they document several approaches towards increasing genetic counselling access in their multidisciplinary cancer service line, an initiative that may present a solution to improving referral access patterns.[20] First, they educated clinical teams (composed of physicians, advanced practice providers, and nurses) on referral standards and improving patient referral uptake.[20] Second, patients were through educating patients with PCa (and their families) on genetic associations with disease severity.[20] Finally, they integrated genitourinary-focused genetic counselling into their multidisciplinary clinic, resulting in a drastic improvement in the number of referrals across the COVID-19 pandemic and onwards.[20] While we detail several potential initiatives to, further research aimed at establishing such initiatives is encouraged and though we suspect the trend observed in this study was due to increasing guidance and awareness, additional research is warranted to firmly establish this.

Another key finding of this study was the low referral rate to genetic counselors by urologists, comprising only 6% (3/49) of referrals for eligible PCa patients in our cohort. This is of particular importance given the recognized challenges in implementing germline testing into daily practice.[12] Previously identified challenges include time constraints, lack of expertise required for adequate counseling, selection of appropriate genetic tests, and accurate interpretation of results.[11,12,22,23] Given that genetic counselors are trained to manage these complexities, they may provide a practical solution for improving the feasibility and quality of the genetic evaluation process for patients and physicians.[12] This low rate of referral is noted in conjunction with a non-existent rate of referral for high/very-high risk of localized disease, for which the urologist would be the initial provider. Several potential hypotheses for this finding exist. Firstly, it may be the case that for patients with advanced (and particularly metastatic) disease urologists may over-rely on medical oncology colleagues for genetic risk stratification and referrals for counselling. Second, this finding may reflect varying familiarity with guidance across specialties, as well as difference in counselling methods potentially resulting in varying uptakes by-specialty. While these hypotheses may explain our findings, the specific underpinnings of this finding were not investigated and warrant investigation. Future interventions aimed at referral practices within our center could include automated referral flags based on pathology results, physician-oriented education, or pre-referral counselling support built into clinic time. Similarly, improving awareness through previously documented initiatives, as well as through incentives (both financial or otherwise) could improve expertise and time limitations where relevant though this hypothesis requires validation.

This study also highlights a potential discrepancy between the number of eligible patients subsequently receiving genetic testing at our institution. Though performed in a separate population, the PRECISION study showed that of a total of 500 men with PCa undergoing biopsy, approximately three percent (3%) of participants demonstrated high risk disease on standard template biopsies.[24] If extrapolated to our

initial population of 6995 patients undergoing biopsy, more than 200 patients would have qualified for a genetic counselling referral based on high-risk disease alone, with only 49/200 (24.5%) of such referrals observed in this study. This finding is likely multifaceted, with socioeconomic, psychological, and practical limitations influencing subsequent testing. Though not specifically investigated, it is entirely possible that during counselling, a shared decision making process was made not to pursue further testing due to limited insurance coverage, financial toxicity, and test-related costs.[25] Also, concerns about revealing the confidentiality of testing results and impact on future insurance coverage and premium costs, as well as discrimination, may contribute to compliance. In the context of this study, these conclusions remain speculative as information pertaining to referral attrition was not collected, and the sample size is modest.

In this analysis, the overall prevalence of PCa-associated genetic variants (2; 4.4%) aligns broadly with previously reported ranges of 4.6–11.8%.[7] While the prevalence of pathogenic variants may appear modest at first glance, results may carry significant prognostic implications for patients.[26–29] Recent advancements in PARP (for BRCA or ATM variants) and immune checkpoint inhibitors (i.e., Niraparib for homologous recombination repair [HRR] deficient tumors) have demonstrated survival benefits for PCa patients harboring pathogenic variants.[26–29] In their phase three clinical trial, Chi et al. specifically investigate 212 patients with metastatic castration-resistant prostate cancer (a population of patients which should receive genetic testing based on referral criteria) harboring HRR gene variants (with and without BRCA 1/2 variants) receiving niraparib and abiraterone acetate.[28] Compared to 211 controls, patients with HRR gene variants and those with BRCA 1/2 variants demonstrated statistically significant improvements in symptomatic progression and progression free survival.[27] Irrespective, this represents a rapidly evolving field of research and findings/clinical guidance may likely change with time.

An additional finding of our study was the documented high prevalence of VUSs (24.4%) observed, detailed in Table A1. Prior investigations by Nicolosi et al. and Fasulo et al. have noted a similar prevalence of VUSs (17.2–23.7%) in their cohorts.[30,31] While such variants may not be conventionally associated with PCa risk at this time, their future associations remain unclear particularly within the context of each variant differing in likelihood of pathogenicity.[32] Irrespective, given their unknown nature, the dangers of over-interpreting such variants may be substantial and result in overtreatment, thus their use in the clinical management of patients discouraged and their prognostic significance uncertain.[32] Given that genetic testing itself may be associated with anxiety and distress for patients, it may be the case that such unrest is exacerbated among patients documented to carry variants with unknown significance (particularly compared to those receiving negative results), though this claim requires validation.[33]

The findings of this study should be considered in light of several limitations inherent to this work. The retrospective nature of this single-institution study introduces selection bias and limits the generalizability of our results. While spanning an extended period, the overall sample size of patients undergoing genetic counseling was relatively modest, particularly considering P/LPV prevalence. Critically, our methodology only captured patients who completed a genetic counseling visit. This means that the true number of referrals placed by urologists could be underestimated if patients did not follow through with appointments, and it may also skew the apparent distribution of referring specialties if certain specialties achieve higher patient compliance with counseling referrals. Similarly, while all of those referred (49; 100%) had indications for genetic testing, this study did not consider how many patients from the initial 6695 biopsies carried an indication. Additionally, providers managing their own genetic testing, possibly via point-of-care testing rather than referring to genetic counseling, or patients pursuing outside-of-system/at-home genetic testing, are uncaptured by this study and limit the scope of our analysis and preclude subsequent conclusions. Despite these limitations, this study offers insights into referral patterns for genetic counseling and subsequent genetic testing outcomes over a 12-year period spanning several iterations of PCa genetic testing guidelines. Using this study as a reference, future research should focus on the identification of key barriers to referral as well as detailing the efficacy of interventions aimed at improving genetic testing referral practices. Furthermore, studies correlating genetic counseling uptake and testing outcomes with subsequent treatment decisions, patient-reported outcomes, and long-term

survival are warranted to further elucidate the clinical impact of integrating genetic evaluation into PCa care.

## Conclusions

In this study, although all patients referred to genetic counselling met established National Comprehensive Cancer Network criteria at the time of referral, urologists only accounted for a minority of referrals, with the majority originating from medical oncologists and patient self-referrals. While the number of referrals to genetic counselling increased over time in parallel with evolving guidance and recommendations, barriers to routine utilization by urologists remain underexplored in contemporary literature. Additionally, while most of the patients in this study did not harbor pathogenic variants, the variants identified by testing may carry significant therapeutic and prognostic implications. As germline testing becomes increasingly relevant for treatment selection and familial risk evaluation practices in PCa, further research is needed to firmly establish the impact of genetic evaluation on treatment decisions, outcomes, and survivorship. Furthermore, given the high observed prevalence of variants of unknown significance, further investigation into their potential roles in prognosis and pathogenesis is encouraged as genetic evaluation practices continue to evolve with time and the emergence of further evidence.

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## Funding Statement

No funding was provided for the study.

## Author Contributions

Ernest A. Morton: concept development, research design, data collection and interpretation, manuscript development, figure/image generation. Reza Lahiji: research design, data collection and interpretation, manuscript development, figure/image generation. Elizabeth Chu: data interpretation, manuscript development. William Luke: data interpretation, manuscript development. Vivian I. Anyaeche: data interpretation, manuscript development. Dattatraya Patil: data collection and analysis. Akanksha Mehta: research designs and manuscript development. Shreyas S. Joshi: research designs and manuscript development. Taylor A. Goodstein: manuscript development. Valentina Grajales: research designs and manuscript development. Mohammad Hajiha: concept development, research design, data interpretation, manuscript development, project management. All authors reviewed and approved the final version of the manuscript.

## Availability of Data and Materials

Data available upon request.

## Ethics Approval

As this study was completed as part of a larger quality improvement project, IRB approval and informed consent were not required.

## Conflicts of Interest

The authors declare no conflicts of interest.

## Appendix A

TABLE A1. **Genetic variants by corresponding pre-biopsy PSAs, Gleason group scores, genetic tests, and labs**

| Genetic variants | Pre-biopsy PSA | Biopsy Gleason group | Genetic test performed | Genetic testing lab |
|---|---|---|---|---|
| **VUS (n = 11)** | | | | |
| *BARD1* | 4.9 | 4 + 4 | CancerNext panel | Ambry |
| *1 in NTHL, 2 in RECQL* | 7.0 | 3 + 4 | Hereditary Cancer gene testing | Invitae |
| *ATM* | 5.8 | 4 + 3 | CancerNext panel | Ambry |
| *SDHAF2* | 0.7 | 3 + 3 | Multicancer panel and RNA gene testing | Invitae |
| *PRKAR1R* | 5.7 | 4 + 3 | Detect panel gene testing | Invitae |
| *POLD1* | 5.0 | 3 + 3 | BRCA/12 with multi-cancer panel gene and RNA testing | Invitae |
| *POLE* | 9.5 | 4 + 3 | Common hereditary cancers panel (detect program) | Invitae |
| *1× APC, 1× ATR, 1× BRIP, 1× FANCA* | 10.8 | 4 + 3 | Detect panel gene testing | Invitae |
| *PALB2* | 353.0 | 5 + 5 | Common hereditary cancers panel (detect program) | Invitae |
| *AXIN2* | 30.9 | 4 + 5 | Multicancer panel gene testing | Invitae |
| *TSC1* | 6.2 | 3 + 4 | Myrisk panel gene testing | Myriad |
| ***FH* variant (n = 2)** | | | | |
| c.698G > A | 6.7 | 3 + 3 | Breast and Gyn cancer Guidelines-Based panel, FH, and HOXB13 | Invitae |
| c.1431_1433dup (p.Lys477dup) | 0.6 | Benign | BRCA1/2 with multi-cancer panel gene testing | Invitae |
| ***MSH2*variant (n = 1)** | | | | |
| c.1786_1788delAAT | 22.0 | 4 + 4 | Specific site analysis | Ambry |
| ***SDHD*variant (n = 1)** | | | | |
| c.242C > T (p.Pro81Leu) | 7.7 | 3 + 4 | SDHD sequence analysis and deletion/duplication testing | Invitae |
| ***BRCA2* (n = 1)** | | | | |
| c.6275_6276del (p.Leu2092Profs*7) | 11.1 | 3 + 3 | BRCA2 sequence analysis and deletion/duplication testing | Invitae |
| ***BARD1* (n = 1)** | | | | |
| c.334C > T (p.Arg112*) | 76.0 | 4 + 5 | Common hereditary cancers panel gene testing | Invitae |

Note. "*" Relates to a stop codon in that gene sequence. Abbreviations: N, number; PSA, prostate specific antigen; RNA, ribonucleic acid; VUS, Variant of Uncertain Significance; PSA, Prostate-Specific Antigen; FH, Fumarate Hydratase; BRCA, Breast Cancer associated gene (BRCA1/2); HOXB13, Homeobox B13; BARD1, BRCA1-associated RING domain 1; ATM, Ataxia Telangiectasia Mutated; SDHAF2, Succinate Dehydrogenase Complex Assembly Factor 2; PRKAR1R, Protein Kinase cAMP-Dependent Type I Regulatory Subunit; POLD1, DNA Polymerase Delta 1; POLE, DNA Polymerase Epsilon; PALB2, Partner and Localizer of BRCA2; AXIN2, Axis Inhibition Protein 2; TSC1, Tuberous Sclerosis Complex 1; MSH2, MutS Homolog 2; SDHD, Succinate Dehydrogenase Complex Subunit D.

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