

Implementation of Germline Testing for Prostate Cancer: Philadelphia Prostate Cancer Consensus Conference 2019

Veda N. Giri, MD^{1,2,3}; Karen E. Knudsen, MBA, PhD³; William K. Kelly, DO¹; Heather H. Cheng, MD, PhD⁴; Kathleen A. Cooney, MD⁵; Michael S. Cookson, MD⁶; William Dahut, MD⁷; Scott Weissman, MS⁸; Howard R. Soule, PhD⁹; Daniel P. Petrylak, MD¹⁰; Adam P. Dicker, MD, PhD¹¹; Saud H. AlDubayan, MD¹²; Amanda E. Toland, PhD¹³; Colin C. Pritchard, MD, PhD¹⁴; Curtis A. Pettaway, MD¹⁵; Mary B. Daly, MD, PhD¹⁶; James L. Mohler, MD¹⁷; J. Kellogg Parsons, MD¹⁸; Peter R. Carroll, MD, MPH¹⁹; Robert Pilarski, MS, MSW²⁰; Amie Blanco, MS²¹; Ashley Woodson, MS¹⁵; Alanna Rahm, PhD²²; Mary-Ellen Taplin, MD¹²; Thomas J. Polascik, MD²³; Brian T. Helfand, MD, PhD²⁴; Colette Hyatt, MS²⁵; Alicia K. Morgans, MD, MPH²⁶; Felix Feng, MD²⁷; Michael Mullane, MD²⁸; Jacqueline Powers, MS²⁹; Raoul Concepcion, MD³⁰; Daniel W. Lin, MD³¹; Richard Wender, MD³²; James Ryan Mark, MD²; Anthony Costello, MBBS³³; Arthur L. Burnett, MD, MBA³⁴; Oliver Sartor, MD³⁵; William B. Isaacs, PhD³⁶; Jianfeng Xu, MD, DrPH²⁴; Jeffrey Weitzel, MD³⁷; Gerald L. Andriole, MD³⁸; Himisha Beltran, MD³⁹; Alberto Briganti, MD, PhD⁴⁰; Lindsey Byrne, MS⁴¹; Anne Calvaresi, DNP²; Thenappan Chandrasekar, MD²; David Y. T. Chen, MD¹⁶; Robert B. Den, MD¹¹; Albert Dobi, PhD⁴²; E. David Crawford, MD⁴³; James Eastham, MD⁴⁴; Scott Eggener, MD⁴⁵; Matthew L. Freedman, MD³⁹; Marc Garnick, MD⁴⁶; Patrick T. Gomella, MD, MPH⁴⁷; Nathan Handley, MD, MBA¹; Mark D. Hurwitz, MD¹¹; Joseph Izes, MD, MS²; R. Jeffrey Karnes, MD⁴⁸; Costas Lallas, MD²; Lucia Languino, PhD³; Stacy Loeb, MD, MSc⁴⁹; Ana Maria Lopez, MD, MPH¹; Kevin R. Loughlin, MD, MBA⁵⁰; Grace Lu-Yao, PhD, MPH¹; S. Bruce Malkowicz, MD⁵¹; Mark Mann, MD²; Patrick Mille, MD¹; Martin M. Miner, MD⁵²; Todd Morgan, MD⁵³; Jose Moreno, MD⁵⁴; Lorelei Mucci, ScD, MPH⁵⁵; Ronald E. Myers, DSW, PhD¹; Sarah M. Nielsen, MS⁴⁵; Brock O'Neil, MD⁵⁶; Wayne Pinover, DO⁵⁷; Peter Pinto, MD⁴⁷; Wendy Poage, MHA⁵⁸; Ganesh V. Raj, MD, PhD⁵⁹; Timothy R. Rebbeck, PhD⁵⁵; Charles Ryan, MD⁶⁰; Howard Sandler, MD, MS⁶¹; Matthew Schiewer, PhD³; E. Michael D. Scott, BSc⁶²; Brittany Szymaniak, PhD, MS⁶³; William Tester, MD¹; Edouard J. Trabulsi, MD²; Neha Vapiwala, MD⁵¹; Evan Y. Yu, MD⁶⁴; Charnita Zeigler-Johnson, PhD, MPH¹; and Leonard G. Gomella, MD²

ASSOCIATED CONTENT

Appendix

Data Supplement

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

Accepted on March 27, 2020 and published at ascopubs.org/journal/jco on June 9, 2020; DOI <https://doi.org/10.1200/JCO.20.00046>

The contents of this manuscript are not to be construed as official or reflecting the views of the Department of Defense, the Uniformed Services University of the Health Sciences, or any other agency of the US Government. This manuscript does not constitute endorsement or implied endorsement on the part of the Department of Defense or any component agency.

abstract

PURPOSE Germline testing (GT) is a central feature of prostate cancer (PCA) treatment, management, and hereditary cancer assessment. Critical needs include optimized multigene testing strategies that incorporate evolving genetic data, consistency in GT indications and management, and alternate genetic evaluation models that address the rising demand for genetic services.

METHODS A multidisciplinary consensus conference that included experts, stakeholders, and national organization leaders was convened in response to current practice challenges and to develop a genetic implementation framework. Evidence review informed questions using the modified Delphi model. The final framework included criteria with strong (> 75%) agreement (Recommend) or moderate (50% to 74%) agreement (Consider).

RESULTS Large germline panels and somatic testing were recommended for metastatic PCA. Reflex testing—initial testing of priority genes followed by expanded testing—was suggested for multiple scenarios. Metastatic disease or family history suggestive of hereditary PCA was recommended for GT. Additional family history and pathologic criteria garnered moderate consensus. Priority genes to test for metastatic disease treatment included *BRCA2*, *BRCA1*, and mismatch repair genes, with broader testing, such as *ATM*, for clinical trial eligibility. *BRCA2* was recommended for active surveillance discussions. Screening starting at age 40 years or 10 years before the youngest PCA diagnosis in a family was recommended for *BRCA2* carriers, with consideration in *HOXB13*, *BRCA1*, *ATM*, and mismatch repair carriers. Collaborative (point-of-care) evaluation models between health care and genetic providers was endorsed to address the genetic counseling shortage. The genetic evaluation framework included optimal pretest informed consent, post-test discussion, cascade testing, and technology-based approaches.

CONCLUSION This multidisciplinary, consensus-driven PCA genetic implementation framework provides novel guidance to clinicians and patients tailored to the precision era. Multiple research, education, and policy needs remain of importance.

J Clin Oncol 38:2798-2811. © 2020 by American Society of Clinical Oncology

INTRODUCTION

The role of germline testing (GT) for prostate cancer (PCA) has increased, with growing precision treatment implications and expanded testing options.^{1,2} A primary driver for GT is now precision therapy for

metastatic disease where genetic results inform options and strategies for targeted treatment, therapeutic planning, and clinical trials.¹⁻⁴ Approximately 12% to 17% of men with metastatic PCA harbor germline mutations, primarily in DNA repair genes, such as

BRCA2, *CHEK2*, *BRCA1*, *ATM*, *PALB2*, and the DNA mismatch repair (MMR) genes,⁵ which are increasingly informing options for poly (ADP-ribose) polymerase (PARP) inhibitors, immune checkpoint inhibitors, platinum chemotherapy, and clinical trials.^{1-4,6} In early-stage disease, emerging data suggest that men with germline *BRCA2* mutations, and possibly *ATM* mutations, have higher rates of upgrading of prostate biopsies while on active surveillance (AS).⁷ GT results are considered increasingly in PCA early detection discussions, particularly for men with *BRCA2* mutations for which data support higher rates of PCA detection, younger age at diagnosis, and more clinically significant disease.⁸⁻¹⁰ Many of the genes that are important for PCA therapy, management, and early detection are associated with hereditary cancer syndromes.¹¹ Pathogenic variants in *BRCA1* and *BRCA2* are associated with hereditary breast and ovarian cancer (HBOC). DNA MMR genes—*MLH1*, *MSH2*, *PMS2*, *MSH6*, and *EPCAM*—are associated with Lynch syndrome.¹¹⁻¹⁶ These and other hereditary cancer syndromes confer risks for multiple cancers that must be addressed for men and their kindred.^{8,16}

As PCA GT has increased, new practice and implementation challenges have emerged in three major areas: expanded options for multigene panels, with a resultant lack of clarity regarding optimized panel use and priority genes to test; variability in guidelines regarding GT indications and genetically based management that incorporates emerging data; and a shortage of genetic services.^{1,17-21} Testing options have expanded rapidly, which include focused, guideline-based, comprehensive, and reflex panels.^{17,18} Panels include genes with strong, limited, and unknown risk for PCA and that yet confer risks for multiple cancers.¹⁸ There is a need for clarity on panel choice and priority genes to test in men with metastatic PCA, nonmetastatic PCA, and men at high risk for PCA that balances the benefits of expanded testing (eg, identifying actionable mutations) with considerations (eg, higher rates of variants of uncertain significance [VUS]).^{3,8,10}

Uniform guidance is also needed regarding GT indications and genetically based PCA management that incorporates rapidly emerging, sometimes conflicting, data. Current National Comprehensive Cancer Network (NCCN) guidelines have variability regarding GT on the basis of pathologic—stage and Gleason/Grade Group—and family history (FH) criteria.^{3,8,9} Management guidance is also needed in multiple areas with consideration of gene-specific outcomes, such as treatment of metastatic disease with variable responses by DNA repair mutations^{1-4,6}; AS discussions that consider strong data for *BRCA2*, but limited data for *BRCA1* and *ATM*⁷; and broader consideration of genes for PCA early detection.^{1,2,11} In particular, strategies for PCA early detection need clarification regarding age to begin screening on the basis of genetic status.^{8,9}

Furthermore, the rising need for PCA GT has created a critical shortage of genetic counseling (GC) services.^{1,19}

Health care providers, such as oncologists and urologists, increasingly are ordering PCA GT to expedite testing for management.^{20,21} Concerns include limited guidance on optimal pretest informed consent, optimal panel testing strategies for comprehensive genetic evaluation, inclusion of personal history and FH, and balancing timely GT with appropriate referral to GC to address patient and family needs.^{1,20,21} As referral of all men to GC for PCA GT is not sustainable, health care and genetic providers need implementation strategies that incorporate alternate genetic evaluation models for the timely and responsible delivery of PCA GT for men and their families.^{1,19}

The 2019 Philadelphia Prostate Cancer Consensus Conference was convened to address challenges in PCA germline evaluation and implementation with attention to evolving genetic and precision medicine data. This meeting was a follow-up to the 2017 Philadelphia Consensus Conference, which focused on the role of GT for inherited PCA risk.¹⁸ The 2019 conference had the following 3 goals: to define optimal GT strategies that incorporate expansion of panel testing options and evolving genetic data, to propose consistent PCA GT indications and management, and to propose alternate genetic evaluation models to address the GC shortage. An expert, consensus-driven genetic implementation framework was developed for health care and genetic providers to streamline GT for PCA in the precision medicine era.

METHODS

Overarching Questions Addressing Implementation Gaps

The following questions were primary drivers of the conceptual framework:

1. Which men should be considered for germline PCA genetic testing?
2. Which panels should be considered and which genes should be prioritized for testing?
3. What PCA-specific recommendations should be considered on the basis of genetic results?
4. What is optimal informed consent for PCA GT?
5. What collaborative strategies may facilitate PCA genetic evaluation between health care and genetic providers?
6. What post-test disclosure strategies are most appropriate on the basis of genetic results?
7. What barriers must be addressed to enhance PCA GT?

Consensus Conference Participants

The Consensus Conference included 97 participants spanning the fields of urology, medical oncology, radiation oncology, clinical genetics, genetic counseling, primary care, pathology, implementation science, population science, epidemiology, and basic science. Patient stakeholders and advocates were active participants. Members of several national organizations, which included NCCN representatives, also participated. Academic and

community practices were represented, and panelists were from multiple regions of the United States, as well as Europe and Australia. The final voting panel included 76 participants (Table 1).

Consensus Process

The modified Delphi model was followed that incorporated elements of the Delphi process as previously published.^{18,22,23} Literature was provided to panel members before the meeting. Multiple expert presentations summarizing evidence relevant to genetic implementation were delivered. Evidence review is summarized in the Data Supplement.

Evidence Review

Thematic topics included: genetic contribution to PCA risk/aggressiveness²⁴⁻⁵⁴; germline mutations by PCA clinical and molecular characteristics^{5,55-66}; PCA clinical multigene testing data^{60,61,67}; germline mutations in diverse populations^{5,24,30,49,61,68-74}; PCA genetic testing capabilities and considerations^{17,75-81} (Fig 1); implementation of GC^{1,3,8,9,17,76,82-93}; NCCN PCA genetic testing guidelines and current variability^{3,8,9}; GT for PCA precision medicine in the metastatic setting^{2,4,6,56,58,94-99}; germline implications for AS of early-stage PCA^{7,35,99,100,101}; and germline implications for PCA early detection.^{8-10,102} Table 2 provides a summary of genetic data for PCA risk and aggressiveness. Full evidence summary is provided in the Data Supplement.

Strength of Consensus

Votes were cast anonymously using a Web-based polling platform. Strength of consensus was $\geq 75\%$ agreement for strong consensus, 50% to 74% agreement for moderate consensus, and $< 50\%$ agreement for lack of consensus.^{22,23}

Development of PCA Genetic Evaluation and Management Framework

A conceptual framework for PCA genetic evaluation and management was developed (Fig 2). Criteria that achieved strong consensus were designated as “Recommend” and those with moderate consensus were designated as “Consider” in the final framework.

RESULTS

Key premises

The following are guiding principles for clinical genetic evaluation:

Premises based on prior literature and Consensus Conference expert guidance:

- In-person GC is a gold standard of genetics practice.^{2,76,82-84}
- Patients' psychosocial needs or preferences should dictate the mode of counseling.^{1,82-84}
- Full FH is important to collect during the genetic evaluation process:^{1,82-84}

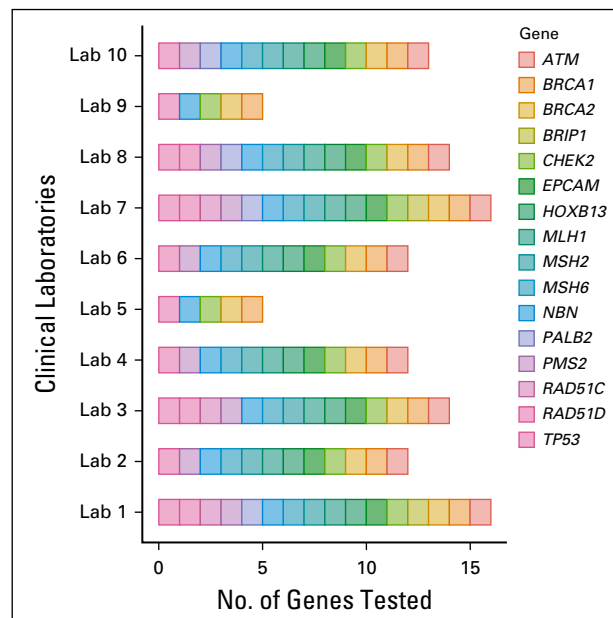


FIG 1. Variability in prostate cancer–specific multigene panels. Genetic testing registry: As of August 2019. Available at: <https://www.ncbi.nlm.gov/gtr/>. Courtesy of Saud AlDubayan, MD.

Premises based on consensus voting:

- Men should engage in informed decision making for genetic testing (Recommend).
- Building collaborations between health care and genetics providers is important for optimal genetic evaluation (Recommend).

1. Which Men Should Be Considered for Germline PCA Genetic Testing?

Gaps addressed. NCCN guidelines (NCCN Prostate Version 4.2019 and NCCN Breast/Ovary Version 3.2019) at the time of the 2019 Consensus meeting had varying indications for PCA GT.^{3,8} Data regarding clinical, pathologic, and FH features were summarized (Data Supplement).

Criteria for testing. Any one of the following criteria may prompt GT:

- **Men with metastatic PCA** (castration resistant or castration sensitive; Recommend).
- **Men with nonmetastatic PCA**—one of the following:
 - Ashkenazi Jewish ancestry (Consider).
 - Advanced disease (T3a or higher; Consider).
 - Intraductal/ductal pathology (Consider).
 - Grade Group 4 (Gleason sum 8) or above (Consider).
- **FH criteria:**
 - **PCA FH criteria:**
 - Men with one brother or father or two or more male relatives with one of the following:
 - Diagnosed with PCA at age < 60 years (Recommend).

- Any of whom died of PCA (Recommend).
- Any of whom had metastatic PCA (Recommend).
- **FH of other cancers:**
 - Two or more cancers in HBOC or Lynch spectrum in any relatives on the same side of the family (especially if diagnosed at age < 50 years; Consider).

Additional considerations. FH consistent with hereditary PCA achieved a strong recommendation for GT. Additional FH criteria were expanded to consider 2 or more cancers in the HBOC or Lynch spectrum to account for limitations in self-reported FH. Genes corresponding to specific cancers are listed in Table 2. Of note, an unremarkable FH does not necessarily negate consideration of GT, particularly for treatment decisions in the metastatic setting.

All pathologic criteria achieved moderate agreement. Universal screening for Lynch syndrome in PCA is not current practice; however, if immunohistochemistry is performed on a prostate specimen revealing loss of the DNA MMR genes, and particularly MSH2, the recommendation is to proceed with GT to determine if the patient has Lynch syndrome given the significant cancer risks and potential treatment implications. Panelists noted that many centers do not report intraductal/ductal pathology or immunohistochemistry for Lynch syndrome markers, which must be addressed with pathologists.

Although multiple unique questions were posed specifically regarding GT for African American men, none met consensus agreement as a result of limited data. Until additional research is completed, testing guidelines as described herein should be applied in under-represented populations.

2. Which Panels Should Be Considered and Which Genes Should Be Prioritized for Testing?

Gaps addressed. Guidance on the use of various gene panels adapted to clinical scenarios is needed given the rapid expansion of panel options and the inclusion of genes with limited association to PCA risk or PCA treatment implications (Fig 1). Furthermore, NCCN guidelines vary regarding genes to test,^{3,8} necessitating consensus prioritization of genes for testing (Data Supplement).

Panels considered. Focused—guidelines-based—panels (approximately 5 to 6 genes), PCA-specific panels (approximately 10 to 15 genes), comprehensive cancer panels (approximately 80 genes), and reflex panels (initial set of genes tested followed by broad gene testing) were considered. Benefits and limitations of various panels were also considered (Data Supplement).

Genes considered. *BRCA1*, *BRCA2*, *HOXB13*, *CHEK2*, *ATM*, *NBN*, *MSH2*, *MSH6*, *MLH1*, *PMS2*, *PALB2*, *BRIP1*, *TP53*, and Fanconi anemia genes were considered.

TABLE 1. Characteristics of Voting Consensus Participants

Participant Characteristic	No. (%)
Primary area of specialty/work (combination of academic and community settings)	
Urology	29 (38)
Medical oncology	13 (17)
Genetic counseling/implementation science	10 (13)
Radiation oncology	5 (7)
Primary care, pathology, and other	9 (12)
Population science/epidemiology	4 (5)
Patient/patient advocate	6 (8)
Geographic region of practice or work	
Northeast United States	26 (34)
Mid-Atlantic United States	14 (18)
Southeast United States	4 (5)
Midwest United States	15 (20)
Southcentral United States	4 (5)
Northwest United States	6 (8)
Southwest United States	3 (4)
Europe, Australia, and Other	4 (5)
Type of region of work	
Urban	55 (71)
Suburban	15 (19)
Rural	2 (3)
Other	5 (6)

TABLE 2. Genetic Contribution to PCA Risk, Aggressiveness, and Proposed Clinical Implications

Gene	Strength of Association for PCA Susceptibility ^a	Risk for Aggressive Disease ^a	Prevalence in Metastatic PCA ^b	Testing for Hereditary Cancer Syndromes and Other Associated Cancers Based on Personal History or FH	Cancer Screening Guidelines for Non-PCAs	PCA-Specific Clinical Impact of Germline Testing: Consensus Conference Summary			
						Implications for PCA Early Detection/PCA Risk Assessment	Implications for AS Decision Making	Metastatic Treatment Options	Clinical Trial Options
<i>ATM</i>	+	++	++	Breast, pancreas	x	+ / + + +	+	++	+++
<i>BRCA1</i>	++	+ / -	+	HBOC syndrome; breast (male and female), ovarian, pancreas, melanoma	x	++		+++	+++
<i>BRCA2</i>	+++	+++	+++	HBOC syndrome; breast (male and female), ovarian, pancreas, melanoma	x	+++	++	+++	+++
<i>HOXB13</i>	+++	-	-	Hereditary PCA		++			
<i>CHEK2</i>	++	+	++	Breast, colon	x				++
<i>MSH2/MSH6</i>	++	+	+	Lynch syndrome; colorectal, ovarian, uterine, gastric, small bowel, pancreas, upper tract urothelial, kidney, sebaceous carcinoma	x	++		++	+++
<i>MLH1/PMS2</i>	+	+ / -	+	Lynch syndrome; colorectal, ovarian, uterine, gastric, small bowel, pancreas, upper tract urothelial, kidney, sebaceous carcinoma	x	+		++	+++
<i>NBN</i>	+ / -	+ / -	+	Breast	x				+
<i>PALB2</i>	-	+	+	Breast, pancreas	x				++
<i>RAD51C-D; BRIP1; Fanconi anemia genes</i>	-	-	+	ovarian (<i>RAD51C/D, BRIP1</i>)	x				++

Abbreviations: AS, active surveillance; FH, family history; HBOC, hereditary breast and ovarian cancer; PCA, prostate cancer.

^aEvidence from case-control, familial, cohort, or clinical studies: strong (+++); moderate (++) ; low (+); conflicting data (+/-); not established (-).

^bHigh prevalence ($\geq 4\%$; +++); moderate prevalence (1% to $< 4\%$; ++); low prevalence ($< 1\%$; +); not reported (-).

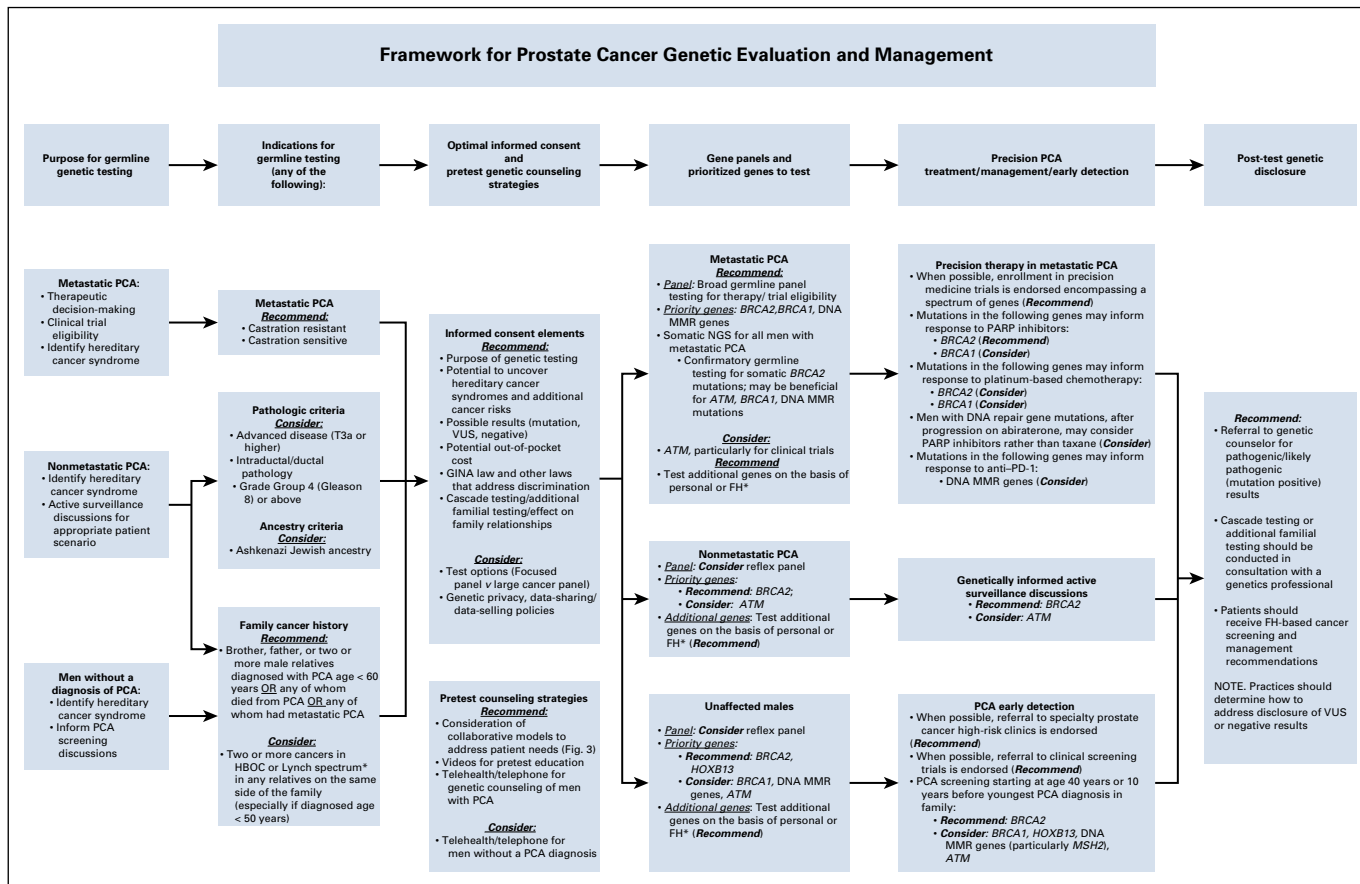


FIG 2. Framework for prostate cancer (PCA) genetic evaluation and management. (*) See Table 2 for personal history or family history (FH) of cancers indicating genes to test. GINA, Genetic Information Nondiscrimination Act; HBOC, hereditary breast and ovarian cancer; MMR, mismatch repair; NGS, next-generation sequencing; PARP, poly (ADP-ribose) polymerase; PD-1, programmed death 1; VUS, variant of uncertain significance.

Panels and genes prioritized for testing:

- **Metastatic PCA:**
 - Comprehensive (large) panel testing for therapy/clinical trial eligibility (Recommend).
 - **Priority germline testing:**
 - *BRCA2/BRCA1* (Recommend).
 - DNA MMR genes (Recommend).
 - *ATM* (Consider).
 - Test additional genes on the basis of personal or FH (Recommend).
 - **Somatic testing:**
 - Somatic next-generation sequencing for all men with metastatic PCA (Recommend).
 - Confirmatory germline testing for somatic mutations:
 - *BRCA2* (Recommend).
 - *BRCA1*, DNA MMR genes, *ATM* (Consider).
 - Test additional genes on the basis of personal or FH (Table 2; Recommend).
- **Nonmetastatic PCA:**
 - Reflex testing may be optimal (Consider).
 - Priority genes particularly to inform AS:
 - *BRCA2* (Recommend).
- **Men without a diagnosis of PCA meeting FH testing criteria:**
 - Reflex testing may be optimal (Consider).
 - Priority genes for risk assessment:
 - *BRCA2* (Recommend).
 - *HOXB13* (Recommend).
 - *BRCA1*, *ATM*, DNA MMR genes (Consider).
 - Test additional genes on the basis of personal or FH (Table 2; Recommend).

Additional considerations. For men with metastatic PCA, broader panel testing may be appropriate, particularly if considering treatment or clinical trial options (Table 2, Fig 2, and Data Supplement). Reflex testing may be considered for all patients, but especially for men with nonmetastatic disease considering AS or men without PCA for early detection, which allows for initial testing of genes that inform management (Data Supplement). Reflex testing also allows for testing of additional genes to account for personal cancer or FH at a later time for comprehensive

genetic evaluation and may also be more amenable to collaborative genetic evaluation models (see below).

Among MMR genes, *MSH2* has the strongest association to PCA; however, it is recognized that *MLH1*, *PMS2*, *MSH6*, and *EPCAM* also need to be tested to establish the diagnosis of Lynch syndrome. Full MMR testing also may be important for treatment consideration or clinical trials in the metastatic setting; therefore, full Lynch syndrome testing is recommended as indicated.

In addition, confirmatory GT is recommended for men with somatic *BRCA2* mutations and may be beneficial for somatic mutations in *BRCA1*, MMR genes, and *ATM* to identify hereditary cancer predisposition. Additional GT beyond these genes may also be recommended on the basis of personal and FH. Consultation with a genetics professional is advised.

3. What PCA-Specific Recommendations Should Be Considered on the Basis of Genetic Results?

Gaps addressed. There is a need for consensus agreement on genetically informed PCA treatment, management, and early detection^{1,2} (Data Supplement). An additional challenge is inconsistency in NCCN genetically based PCA early detection recommendations regarding which genes to consider and the age at which to begin screening^{8,9} (Data Supplement).

Genetically based recommendations. Genes considered included *BRCA1*, *BRCA2*, *HOXB13*, *CHEK2*, *ATM*, *NBN*, *MSH2*, *MSH6*, *MLH1*, *PMS2*, *PALB2*, *BRIP1*, *TP53*, and Fanconi anemia genes.

- **Metastatic PCA:** GT to inform precision therapy:
 - Enrollment of men with PCA in precision medicine trials is endorsed (Recommend).
 - Mutations in the following genes may inform response to PARP inhibitors:
 - *BRCA2* (Recommend).
 - *BRCA1* (Consider).
 - Mutations in the following genes may inform response to platinum-based chemotherapy:
 - *BRCA2* (Consider).
 - *BRCA1* (Consider).
 - Men with DNA repair gene mutations, after progression on abiraterone, may proceed with PARP inhibitor rather than taxane (Consider).
 - Germline mutations in the following genes may inform response to anti-programmed death 1 (PD-1) therapy:
 - DNA MMR genes (Consider).
 - NOTE. The US Food and Drug Administration has granted accelerated approval for anti-PD-1 therapy for microsatellite instability-high/MMR-deficient tumors.
- **Nonmetastatic PCA:** to inform AS discussions:
 - *BRCA2* (Recommend).
 - *ATM* (Consider).

- **Men without a PCA diagnosis to inform PCA early detection:**

- Referral to specialty PCA high-risk clinics and/or early detection trials was endorsed (Recommend).
- PCA early detection starting at age 40 years or 10 years before the youngest PCA diagnosis in family:
 - *BRCA2* (Recommend).
 - *BRCA1*, *HOXB13*, *ATM*, and DNA MMR genes (particularly *MSH2*; Consider).

Additional considerations. In the metastatic setting, a broad spectrum of genes may be important in determining clinical trial eligibility, and emerging data should continue to refine recommendations. *ATM* garnered consideration for testing, primarily for clinical trial eligibility; however, the panel did not feel that there was sufficient data to endorse *ATM* for informing therapy to PARP inhibitors off study because of the limited independent association to PARP inhibitor response at this time (Data Supplement). *ATM* also garnered moderate consensus for informing AS, but there are limited data at this time (Data Supplement).

For anti-PD-1 therapy, the US Food and Drug Administration has granted accelerated approval for tumors that are microsatellite instability-high or MMR deficient. The panel had moderate consensus regarding a definitive recommendation for anti-PD-1 therapy off study for men with germline MMR mutations, with stronger consideration for clinical trials.

Regarding AS discussions, clinicopathologic criteria, age, and overall health must be considered. *BRCA1* did not achieve consensus for inclusion in AS as a result of limited data for PCA aggressiveness (Data Supplement). Polygenic risk score data were reviewed⁷⁷⁻⁸¹ and did not achieve consensus.

4. What Is Optimal Informed Consent for PCA GT?

Gaps addressed. Current practice guidelines do not provide guidance to health care providers regarding optimal informed consent for PCA GT.

Optimal pretest informed consent elements. Ethical considerations of GC were reviewed (Data Supplement). The following elements garnered strong or moderate consensus to discuss with men before GT (Fig 2 and Table 3):

- Recommend discussing: (1) the purpose of GT; (2) the possibility of uncovering hereditary cancer syndromes; (3) potential types of test results; (4) the potential to uncover additional cancer risks; (5) potential out-of-pocket cost; (6) Genetic Information Non-discrimination Act law and other laws that address genetic discrimination; and (7) cascade testing/additional familial testing.
- Consider discussing: (1) multigene panel options; (2) data sharing/data selling policies of genetic laboratories; and (3) the privacy of genetic tests.

TABLE 3. Priority Elements of Informed Consent for Prostate Cancer Germline Testing

Elements of Informed Consent	Description
Purpose of germline testing	For precision therapy, early detection strategies, and/or to identify hereditary cancer syndrome/risk
Possibility of uncovering hereditary cancer syndromes	Based on FH, testing may include BRCA1 and BRCA2 (associated with hereditary breast and ovarian cancer) or DNA mismatch repair genes (associated with Lynch syndrome; Table 2). Other hereditary syndromes may also be identified.
Panel options	Various multigene panels may be considered for testing (focused PCA panel v large cancer panel v reflex testing); benefits and risks of each option must be discussed, such as cancer risks uncovered, higher rates of VUS with larger panels, or availability of guidelines for management (Data Supplement).
Potential types of test results	Three main types of results should be discussed, including mutation (pathogenic/likely pathogenic variant), VUS, negative, along with implications of these results on management.
Potential to uncover additional cancer risks	Multiple gene-specific cancer risks may be identified beyond PCA risk that affects men and their families (Table 2).
Potential out-of-pocket cost	Not all insurance plans cover genetic testing for PCA. Some mandate referral to GC. It is important to check with the insurance plan.
Genetic Information Nondiscrimination Act law and other laws that address genetic discrimination	Discuss coverage for health insurance and most employment scenarios. Discuss the lack of coverage for life insurance, long-term care, and disability insurance.
Cascade testing/additional familial testing	Testing blood relatives for pathogenic variants or additional genetic testing on the basis of family history; worry and anxiety that may result from hereditary cancer testing; effect on family relationships
Data-sharing/data-selling policies of genetic laboratories	Each genetic testing laboratory may have unique data-sharing and data-selling policies that patents must be aware of.
Privacy of genetic tests	Protection of genetic data from data breach or access by third parties must be discussed.

Abbreviations: FH, family history; GC, genetic counseling; PCA, prostate cancer; VUS, variant of uncertain significance.

Additional considerations. These elements of pretest informed consent apply to all men who are considering PCA GT^{76,82-84} (Fig 2). Such GC aids as handouts or videos may be useful to deliver this information. However, informed consent is a process during which patients have opportunities to ask questions^{76,82-84}; therefore, a question-and-answer process must be available before testing. Clinicians without specific training/expertise in GC/GT are urged to refer patients to GC before ordering GT. Furthermore, it is important to remain current on the ethics/informed consent process for GT because of the rapidly evolving nature of precision medicine.

5. What Collaborative Strategies May Facilitate PCA Genetic Evaluation Between Health Care and Genetic Providers?

Gaps addressed. Multidisciplinary guidance on the implementation of collaborative models between health care providers and GC is currently lacking.¹⁰³ There is a need to address alternate GC models for timely GT with attention to appropriate pretest informed consent and comprehensive evaluation.

Alternate genetic evaluation delivery strategies. The following strategies were endorsed (Data Supplement and Fig 3):

- Practices should consider multiple models to address patients' needs (Fig 3), including point-of-care models

with limited or full pretest FH collection as well as traditional model with upfront referral to GC (Recommend).

- Videos may be useful to deliver pretest informed consent (Recommend).
- In point-of-care models, reflex genetic testing may be optimal to enable additional testing on the basis of personal/FH (Consider).
- Telehealth/telephone delivery of GC is a suitable alternative to in-person GC (Recommend for men with PCA; Consider for unaffected males).

Additional considerations. If limited pretest FH is collected, practices must proactively address the collection of FH in the post-test setting. Reflex testing enables future testing to account for personal/FH. Telehealth/telephone GC was endorsed to address geographic barriers to GC, although patient outcomes data in males are lacking. Key process questions for practices to consider when implementing point-of-care versus traditional GC models were discussed (Data Supplement).

6. What Post-Test Disclosure Strategies Are Most Appropriate Based on Genetic Results?

Gaps addressed. Joint guidance from oncologists, urologists, and genetic counselors for referral to GC is currently lacking.

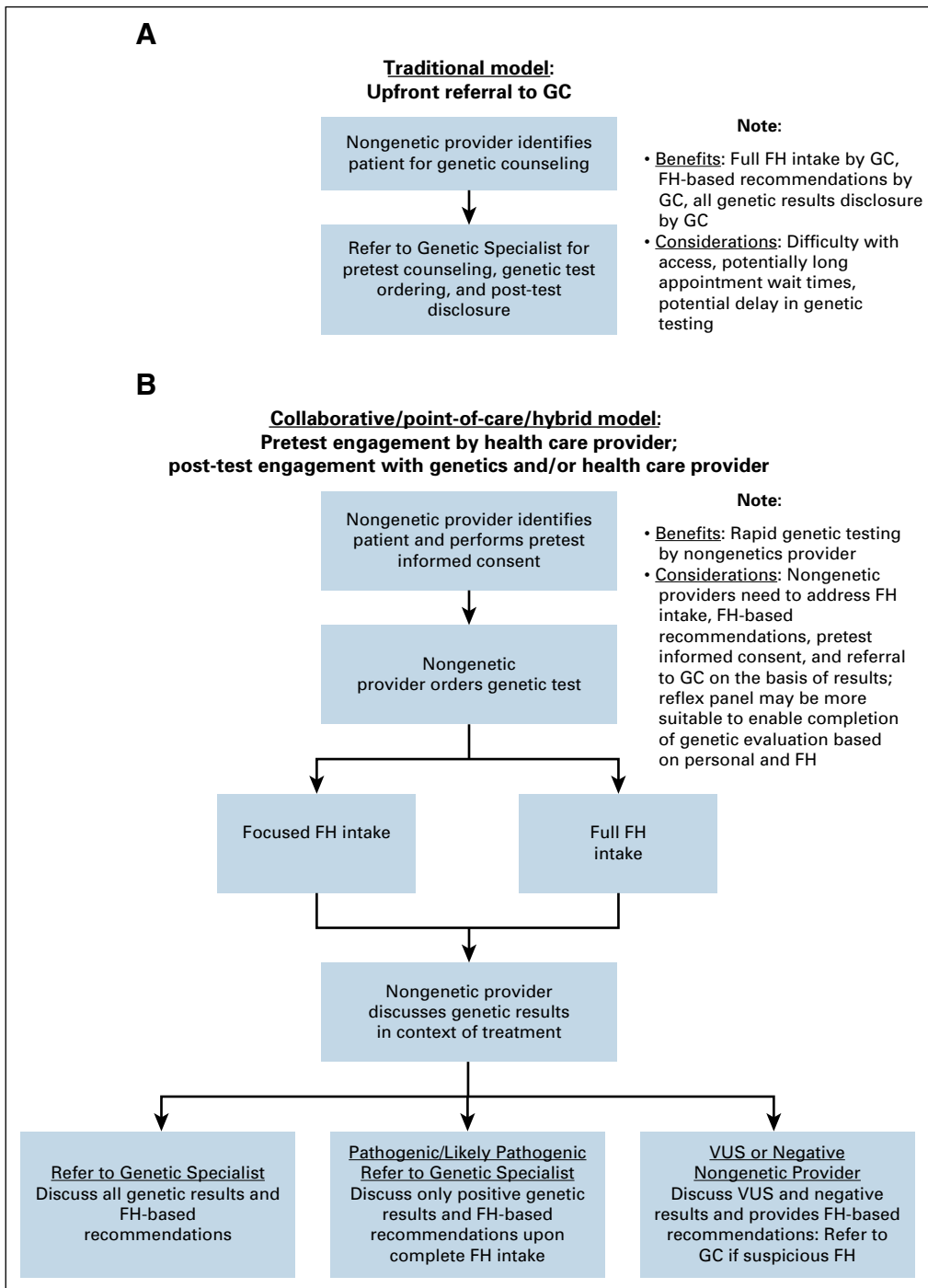


FIG 3. Models of collaboration between genetics and health care practices for prostate cancer genetic evaluation. FH, family history; GC, genetic counseling.

Optimal post-test disclosure strategies:

- Referral to a GC for pathogenic/likely pathogenic results (Recommend).
- Patients should receive FH-based recommendations, either in health care or genetic practices (Recommend).
- Cascade/additional familial testing should be conducted in consultation with a genetic professional (Recommend).

Additional considerations. There was no consensus regarding referral of men with VUS or negative results; therefore, providers will need to determine their ability to discuss VUS results and FH-based recommendations. VUS reclassification to “pathogenic/likely pathogenic” and subsequent management are critical for ordering providers to consider and may support the referral of select men with suspicious VUS to GC. Men with FH of cancers may also warrant referral to GC.

7. What Barriers Must Be Addressed to Enhance PCA GT?

Gaps addressed. Multiple practice, research, and policy gaps pose barriers to PCA GT.

Areas in need of additional attention. The following areas achieved strong or moderate consensus to address:

- Genetic education for providers not formally trained in cancer genetics/genetic counseling (Appendix Table A1, online only, and Data Supplement).
- Barriers to implementation of PCA GT (Appendix Table A2, online only).
- Research priorities (Appendix Table A3, online only).

DISCUSSION

As GT for PCA has rapidly increased, responsible implementation of testing and management are of primary concern.^{1,2,19,23} Current practice challenges that pose barriers to operationalizing PCA GT include the variability in testing indications and genetically based management, the need for guidance on panels and priority genes to test, and guidance regarding alternate evaluation models to address GC demand. The 2019 Philadelphia Prostate Cancer Consensus Conference was a focused attempt to address these critical challenges and practice gaps by developing a first-in-field working framework for PCA genetic evaluation, management, and implementation informed by best evidence and expert guidance.

The strength of the consensus framework is the creation of a unified approach regarding GT indications, genetically informed management and treatment, and the integration of GC. Multiple aspects of the framework had strong evidence and strong expert agreement to deem a definitive action of “Recommend”. The strongest recommendations encompassed testing all men with metastatic PCA or men with FH suggestive of hereditary PCA. Priority genes for testing included *BRCA2*, *BRCA1*, and the DNA MMR genes in metastatic disease to inform treatment or clinical trials; *BRCA2* for AS discussions; and *BRCA2* and *HOXB13* for PCA early detection discussions. This was the first formal, multidisciplinary endorsement for broad panel testing among men with metastatic PCA, recognizing that genetic information may enable men to enroll in clinical trials. Consensus emerged regarding strategies for PCA early detection on the basis of genetic status. For male carriers of *BRCA2*, a recommendation was made to begin PSA screening at age 40 years or 10 years before the youngest PCA diagnosis in a family and is modeled after colorectal cancer guidelines.¹⁶

An important aspect to the genetic evaluation framework was the integration of care processes and GC to account for the increasing need for GC. Strong recommendations were made for optimal pretest informed consent. Recommended strategies to deliver GC included collaborative GC models, videos, and telehealth to facilitate GT through health care practices and to collaborate with GC. Reflex testing

garnered moderate consensus and may be considered, particularly when using collaborative counseling models to enable upfront testing by health care providers, followed by testing additional genes using GC for comprehensive genetic evaluation. In the post-test setting, strong recommendations were made to refer all men with pathogenic mutations to GC, to conduct cascade testing of relatives under the care of genetics professionals, and to determine the delivery of FH-based recommendations.

The panel dealt with many uncertainties in recommendations which garnered moderate consensus. Whereas many genes have a lower level of evidence for PCA risk, aggressiveness, or treatment response, several clinically available multigene panels include lower evidence genes. To indicate these nuances in limited data or moderate consensus, many criteria were designated as “Consider” in the framework. Pathologic criteria for testing, such as disease stage, intraductal/ductal histology, or Grade Group ≥ 4 , garnered moderate consensus and therefore are included as suggestive criteria for testing.^{63,65,66} Ashkenazi Jewish ancestry as a standalone criterion achieved moderate consensus, but may be a stronger consideration for testing for men with higher Gleason score per current NCCN guidelines.⁸ Whereas PCA has been linked with HBOC and Lynch syndrome, a working definition of familial features that increase the likelihood of detecting germline mutations is needed. As such, having two or more relatives with cancers in the HBOC or Lynch syndrome spectrum garnered moderate consensus as standalone criteria and may be considered for GT on the basis of patient preference and insurance coverage.

Priority genes to test also presented challenges, particularly regarding *ATM*, DNA MMR genes, and *HOXB13*. Initial data have reported that men with *ATM* mutations experienced clinical response to PARP inhibitors⁹⁴; however, follow-up studies have reported a limited independent effect of *ATM*.⁹⁹ Similarly, studies in AS had limited association of *ATM* mutations alone with upgrading of biopsies.⁷ Until additional data are available, *ATM* was given a designation of “Consider” for testing, recognizing the potential for clinical trial options for *ATM* carriers. Additional uncertainties were encountered regarding prioritizing MMR genes for GT. Among MMR genes, *MSH2* has the highest reported association to PCA.⁴¹ Although other MMR genes have lower or limited association to PCA, the potential to uncover Lynch syndrome and clinical trial eligibility drove the suggestion to consider full Lynch syndrome testing. *MSH2* status may be more informative for PCA early detection discussions.⁴¹ *HOXB13* has strong association to PCA risk and early-onset disease, though screening outcomes data are limited. Therefore, the consensus panel recommended testing for *HOXB13* and to consider the results in early detection discussions. Overall, *BRCA1*, *HOXB13*, and MMR genes were designated as “Consider”

for beginning screening at age 40 years or 10 years before the youngest PCA diagnosis in the family because of the currently limited screening data.⁹ Data from screening studies, such as IMPACT and the National Cancer Institute (ClinicalTrials.gov identifier: [NCT03805919](https://clinicaltrials.gov/ct2/show/study/NCT03805919)), will be important to reconsider strengthening these recommendations.¹⁰ However, this is the first time that screening strategies based on a larger genetic spectrum have been proposed. Additional research in African American males is

vitaly needed. Future consideration of circulating tumor and cell-free DNA is also warranted.

In conclusion, the 2019 Consensus Conference created the first multidisciplinary PCA genetic implementation framework tailored to the precision medicine era. The framework, which importantly had input from NCCN panel leaders, provides guidance to a spectrum of providers to facilitate timely and responsible PCA GT for the benefit of men and their families.

AFFILIATIONS

- ¹Department of Medical Oncology, Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
- ²Department of Urology, Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
- ³Department of Cancer Biology, Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
- ⁴Department of Medicine, University of Washington, and Fred Hutchinson Cancer Research Center, Division of Clinical Research, Seattle, WA
- ⁵Duke University School of Medicine and Duke Cancer Institute, Durham, NC
- ⁶University of Oklahoma College of Medicine, Norman, OK
- ⁷Genitourinary Malignancies Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD
- ⁸National Society of Genetic Counselors, Chicago, IL
- ⁹Prostate Cancer Foundation, Santa Monica, CA
- ¹⁰Yale Cancer Center, New Haven, CT
- ¹¹Department of Radiation Oncology, Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
- ¹²Dana-Farber Cancer Institute, Boston, MA
- ¹³Department of Cancer Biology and Genetics, The Ohio State University Comprehensive Cancer Center, Columbus, Ohio
- ¹⁴Department of Laboratory Medicine, University of Washington, Seattle, WA
- ¹⁵The University of Texas MD Anderson Cancer Center, Houston, TX
- ¹⁶Fox Chase Cancer Center, Philadelphia, PA
- ¹⁷Roswell Park Comprehensive Cancer Center, Buffalo, NY
- ¹⁸Moore's UC San Diego Comprehensive Cancer Center, San Diego, CA
- ¹⁹Department of Urology, University of California, San Francisco, San Francisco, CA
- ²⁰James Comprehensive Cancer Center and Department of Internal Medicine, The Ohio State University, Columbus, OH
- ²¹University of California, San Francisco, Cancer Genetics and Prevention Program, San Francisco, CA
- ²²Center for Health Research, Genomic Medicine Institute, Geisinger, Danville, PA
- ²³Duke University Medical Center, Durham, NC
- ²⁴North Shore University Health System, Evanston, IL
- ²⁵Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
- ²⁶Northwestern University, Chicago, IL
- ²⁷Departments of Radiation Oncology, Urology, and Medicine, University of California, San Francisco, San Francisco, CA
- ²⁸Advocate Aurora Health, Milwaukee, WI
- ²⁹University of Pennsylvania, Basser Center for BRCA, Philadelphia, PA
- ³⁰Integra Connect, West Palm Beach, FL
- ³¹University of Washington, Seattle, WA
- ³²American Cancer Society, Atlanta, GA
- ³³Urology at Royal Melbourne Hospital, North Melbourne, VIC, Australia
- ³⁴Johns Hopkins Medical Institutions, Baltimore, MD
- ³⁵Tulane University, New Orleans, LA
- ³⁶Brady Urological Institute, Johns Hopkins Medicine, Baltimore, MD

- ³⁷City of Hope Comprehensive Cancer Center, Duarte, CA
- ³⁸Washington University School of Medicine, St Louis, MO
- ³⁹Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA
- ⁴⁰Unit of Urology, Division of Oncology, Urological Research Institute, IRCCS Ospedale San Raffaele, Milan, Italy
- ⁴¹The Ohio State University, Columbus, OH
- ⁴²Henry Jackson Foundation for the Advancement of Military Medicine, Center for Prostate Disease Research, Department of Surgery, Uniformed Services University and the Walter Reed National Military Medical Center, Bethesda, MD
- ⁴³University of California, San Diego, La Jolla, CA
- ⁴⁴Memorial Sloan Kettering Cancer Center, New York, NY
- ⁴⁵University of Chicago, Chicago, IL
- ⁴⁶Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA
- ⁴⁷National Cancer Institute, National Institutes of Health, Bethesda, MD
- ⁴⁸Mayo Clinic, Rochester, MN
- ⁴⁹Department of Urology and Population Health, New York University and Manhattan Veterans Affairs, New York, NY
- ⁵⁰Harvard Medical School, Boston, MA
- ⁵¹University of Pennsylvania, Philadelphia, PA
- ⁵¹Brown University, Providence, RI
- ⁵³University of Michigan, Ann Arbor, MI
- ⁵⁴Midlantic Urology, Phoenixville, PA
- ⁵⁵Department of Epidemiology, Harvard TH Chan School of Public Health, Boston MA
- ⁵⁶University of Utah, Huntsman Cancer Institute, Salt Lake City, UT
- ⁵⁷Abington-Jefferson Hospital, Abington, PA
- ⁵⁸Prostate Conditions Education Council, Elizabeth, CO
- ⁵⁹University of Texas Southwestern Medical Center at Dallas, Dallas, TX
- ⁶⁰University of Minnesota and Masonic Cancer Center, Madison, WI
- ⁶¹Cedars-Sinai Medical Center, Los Angeles, CA
- ⁶²Prostate Cancer International, Virginia Beach, VA
- ⁶³Northwestern Medical Group, Urology Department, Chicago, IL
- ⁶⁴University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA

CORRESPONDING AUTHOR

Veda N. Giri, MD, Cancer Risk Assessment and Clinical Cancer Genetics, Department of Medical Oncology, Sidney Kimmel Cancer Center, Thomas Jefferson University, 1025 Walnut St, Suite 1015, Philadelphia, PA 19107; Twitter: @KimmelCancerCtr, @vedangiri, @SKCCDirector, e-mail: veda.giri@jefferson.edu.

SUPPORT

Supported by National Institutes of Health Cancer Center Support Grant 5P30CA056036-19, Foundation Medicine, Myriad, Bayer, Clovis Oncology, BioReference Laboratories, Ferring Pharmaceuticals, Philadelphia Father's Day Run, Invitae, AstraZeneca, Janssen Oncology, Roche, UroSeq, Color, OncLive, Physician Education Resource, and MDX Health.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI <https://doi.org/10.1200/JCO.20.00046>.

AUTHOR CONTRIBUTIONS

Conception and design: Veda N. Giri, Karen E. Knudsen, William K. Kelly, William Dahut, Howard R. Soule, Adam P. Dicker, Amanda E. Toland, Mary B. Daly, Peter R. Carroll, Amie Blanco, Ashley Woodson, Mary-Ellen Taplin, Jacqueline Powers, Richard Wender, Anthony Costello, Anne Calvaresi, Thenappan Chandrasekar, James Eastham, Costas Lallas, Ana Maria Lopez, Mark Mann, Martin M. Miner, Lorelei Mucci, Ronald E. Myers, Brock O'Neil, Peter Pinto, Timothy R. Rebbeck, Charles Ryan, E. Michael D. Scott, Leonard G. Gomella

Administrative support: Leonard G. Gomella

Provision of study materials or patients: Veda N. Giri, Leonard G. Gomella

Collection and assembly of data: Veda N. Giri, William K. Kelly, Heather H. Cheng, Kathleen A. Cooney, Scott Weissman, Adam P. Dicker, Saud AlDubayan, Amanda E. Toland, Colin C. Pritchard, Curtis A. Pettaway, Mary B. Daly, James L. Mohler, Peter R. Carroll, Ashley Woodson, Alanna Rahm, Mary-Ellen Taplin, Thomas J. Polascik, Brian T. Helfand, Colette Hyatt, Alicia K. Morgans, Felix Feng, Raoul Concepcion, Daniel W. Lin, Richard Wender, James Ryan Mark, William B. Isaacs, Jianfeng Xu, Jeffrey Weitzel, Lindsey Byrne, Anne Calvaresi, Thenappan Chandrasekar, Patrick T. Gomella, Nathan Handley, Joseph Izes, R. Jeffrey Karnes, Ana Maria Lopez, S. Bruce Malkowicz, Mark Mann,

Patrick Mille, Sarah M. Nielsen, Brock O'Neil, Peter Pinto, Wendy Poage, Timothy R. Rebbeck, Howard Sandler, E. Michael D. Scott, Brittany Szymaniak, Neha Vapiwala, Charnita Zeigler-Johnson, Leonard G. Gomella

Data Analysis and interpretation: Veda N. Giri, William K. Kelly, Heather H. Cheng, Kathleen A. Cooney, Michael S. Cookson, William Dahut, Scott Weissman, Daniel P. Petrylak, Colin C. Pritchard, Curtis A. Pettaway, James L. Mohler, J. Kellogg Parsons, Peter R. Carroll, Robert Pilarski, Ashley Woodson, Alanna Rahm, Mary-Ellen Taplin, Thomas J. Polascik, Brian T. Helfand, Alicia K. Morgans, Felix Feng, Michael Mullane, Richard Wender, Arthur L. Burnett, Oliver Sartor, Jeffrey Weitzel, Gerald L. Andriole, Himisha Beltran, Alberto Briganti, David Y. T. Chen, Robert B. Den, Albert Dobi, E. David Crawford, James Eastham, Scott Eggner, Matthew L. Freedman, Marc Garnick, Mark D. Hurwitz, Joseph Izes, R. Jeffrey Karnes, Lucia Languino, Stacy Loeb, Ana Maria Lopez, Kevin R. Loughlin, Grace Lu-Yao, S. Bruce Malkowicz, Mark Mann, Patrick Mille, Martin M. Miner, Todd Morgan, Jose Moreno, Wayne Pinover, Peter Pinto, Ganesh V. Raj, Matthew Schiewer, William Tester, Edouard J. Trabulsi, Neha Vapiwala, Evan Y. Yu, Leonard G. Gomella

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

ACKNOWLEDGMENT

The authors are grateful to patients and patient advocates who participated in the Consensus Conference: Buehler J., Hegedus A., Kaye P., Martin S., and Waxman S.P.

REFERENCES

- Giri VN, Hyatt C, Gomella LG: GT for men with prostate cancer: Navigating an expanding new world of genetic evaluation for precision therapy and precision management. *J Clin Oncol* 37:1455-1459, 2019
- Cheng HH, Sokolova AO, Schaeffer EM, et al: Germline and somatic mutations in prostate cancer for the clinician. *J Natl Compr Canc Netw* 17:515-521, 2019
- National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology: Prostate cancer (version 4.2019). https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf
- Morgans AK, Szymaniak BM: Genetically-informed treatment for advanced and metastatic prostate cancer. *Can J Urol* 26:54-56, 2019
- Pritchard CC, Mateo J, Walsh MF, et al: Inherited DNA-repair gene mutations in men with metastatic prostate cancer. *N Engl J Med* 375:443-453, 2016
- Carlo MI, Giri VN, Antonarakis ES, et al: Evolving intersection between inherited cancer genetics and therapeutic clinical trials in prostate cancer: A white paper from the Germline Genetics Working Group of the Prostate Cancer Clinical Trials Consortium. *JCO Precis Oncol* 10.1200/PO.18.00060
- Carter HB, Helfand B, Mamawala M, et al: Germline mutations in ATM and BRCA1/2 are associated with grade reclassification in men on active surveillance for prostate cancer. *Eur Urol* 75:743-749, 2019
- National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology: Genetic/familial high-risk assessment: Breast, ovarian, and pancreatic (version 3.2019). https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf
- National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology: Prostate cancer early detection (version 1.2019). https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf
- Page EC, Bancroft EK, Brook MN, et al: Interim results from the IMPACT study: Evidence for prostate-specific antigen screening in BRCA2 mutation carriers. *Eur Urol* 76:831-842, 2019
- National Cancer Institute: PDQ cancer information summaries: Genetics. <https://www.cancer.gov/publications/pdq/information-summaries/genetics>
- Mersch J, Jackson MA, Park M, et al: Cancers associated with BRCA1 and BRCA2 mutations other than breast and ovarian. *Cancer* 121:269-275, 2015
- Ryan S, Jenkins MA, Win AK: Risk of prostate cancer in Lynch syndrome: A systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev* 23:437-449, 2014
- National Cancer Institute: Genetics of breast and gynecologic cancers (PDQ) –Health professional version. <https://www.cancer.gov/types/breast/hp/breast-ovarian-genetics-pdq>
- National Cancer Institute: Genetics of colorectal cancer (PDQ) –Health professional version. <https://www.cancer.gov/types/colorectal/hp/colorectal-genetics-pdq>
- National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology: Genetic/familial high-risk assessment: Colorectal (version 2.2019). https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf
- Hall MJ, Forman AD, Pilarski R, et al: Gene panel testing for inherited cancer risk. *J Natl Compr Canc Netw* 12:1339-1346, 2014
- Giri VN, Knudsen KE, Kelly WK, et al: Role of genetic testing for inherited prostate cancer risk: Philadelphia Prostate Cancer Consensus Conference 2017. *J Clin Oncol* 36:414-424, 2018
- Abacan M, Alsubaie L, Barlow-Stewart K, et al: The global state of the genetic counseling profession. *Eur J Hum Genet* 27:183-197, 2019
- Paller CJ, Antonarakis ES, Beer TM, et al: Germline genetic testing in advanced prostate cancer, practices and barriers: Survey results from the Germline Genetics Working Group of the Prostate Cancer Clinical Trials Consortium. *Clin Genitourin Cancer* 17:275.e1-282.e1, 2019
- Giri VN: Genetic education and practice considerations of non-genetic providers. *Can J Urol* 26:44-45, 2019

22. Goggins M, Overbeek KA, Brand R, et al: Management of patients with increased risk for familial pancreatic cancer: Updated recommendations from the International Cancer of the Pancreas Early detection (CAPS) Consortium. *Gut* 69:7-17, 2020
23. Gomella LG, Knudsen KE, Giri VN: Introduction to the 2019 Philadelphia Prostate Cancer Consensus Program: Implementation of genetic testing for inherited prostate cancer. *Can J Urol* 26:1-4, 2019
24. National Cancer Institute: Genetics of prostate cancer (PDQ) –Health professional version. <https://www.cancer.gov/types/prostate/hp/prostate-genetics-pdq>
25. Breast Cancer Linkage Consortium: Cancer risks in BRCA2 mutation carriers. *J Natl Cancer Inst* 91:1310-1316, 1999
26. Thompson D, Easton DF; Breast Cancer Linkage Consortium: Cancer incidence in BRCA1 mutation carriers. *J Natl Cancer Inst* 94:1358-1365, 2002
27. Tryggvadóttir L, Vidarsdóttir L, Thorgeirsson T, et al: Prostate cancer progression and survival in BRCA2 mutation carriers. *J Natl Cancer Inst* 99:929-935, 2007
28. Nyberg T, Frost D, Barrowdale D, et al: Prostate cancer risks for male BRCA1 and BRCA2 mutation carriers: A prospective cohort study. *Eur Urol* 77:24-35, 2020
29. Edwards SM, Evans DG, Hope Q, et al: Prostate cancer in BRCA2 germline mutation carriers is associated with poorer prognosis. *Br J Cancer* 103:918-924, 2010
30. Gallagher DJ, Gaudet MM, Pal P, et al: Germline BRCA mutations denote a clinicopathologic subset of prostate cancer. *Clin Cancer Res* 16:2115-2121, 2010
31. Thorne H, Willems AJ, Niedermayr E, et al: Decreased prostate cancer-specific survival of men with BRCA2 mutations from multiple breast cancer families. *Cancer Prev Res (Phila)* 4:1002-1010, 2011
32. Castro E, Goh C, Olmos D, et al: Germline BRCA mutations are associated with higher risk of nodal involvement, distant metastasis, and poor survival outcomes in prostate cancer. *J Clin Oncol* 31:1748-1757, 2013
33. Akbari MR, Wallis CJ, Toi A, et al: The impact of a BRCA2 mutation on mortality from screen-detected prostate cancer. *Br J Cancer* 111:1238-1240, 2014
34. Castro E, Goh C, Leongamornlert D, et al: Effect of BRCA mutations on metastatic relapse and cause-specific survival after radical treatment for localised prostate cancer. *Eur Urol* 68:186-193, 2015
35. Na R, Zheng SL, Han M, et al: Germline mutations in ATM and BRCA1/2 distinguish risk for lethal and indolent prostate cancer and are associated with early age at death. *Eur Urol* 71:740-747, 2017
36. Boyle J, Cooney KA: DNA repair genes: Contributions to prostate cancer predisposition and aggressiveness. *Can J Urol* 26:10-11, 2019
37. Ewing CM, Ray AM, Lange EM, et al: Germline mutations in HOXB13 and prostate-cancer risk. *N Engl J Med* 366:141-149, 2012
38. Xu J, Lange EM, Lu L, et al: HOXB13 is a susceptibility gene for prostate cancer: Results from the International Consortium for Prostate Cancer Genetics (ICPCG). *Hum Genet* 132:5-14, 2013
39. Salinas CA, Tsodikov A, Ishak-Howard M, et al: Prostate cancer in young men: An important clinical entity. *Nat Rev Urol* 11:317-323, 2014
40. Bauer CM, Ray AM, Halstead-Nussloch BA, et al: Hereditary prostate cancer as a feature of Lynch syndrome. *Fam Cancer* 10:37-42, 2011
41. Dominguez-Valentin M, Sampson JR, Seppälä TT, et al: Cancer risks by gene, age, and gender in 6350 carriers of pathogenic mismatch repair variants: Findings from the Prospective Lynch Syndrome Database. *Genet Med* 22:15-25, 2020
42. Angèle S, Falconer A, Edwards SM, et al: ATM polymorphisms as risk factors for prostate cancer development. *Br J Cancer* 91:783-787, 2004
43. Meyer A, Wilhelm B, Dörk T, et al: ATM missense variant P1054R predisposes to prostate cancer. *Radiother Oncol* 83:283-288, 2007
44. Schumacher FR, Al Olama AAA, Berndt SI, et al: Association analyses of more than 140,000 men identify 63 new prostate cancer susceptibility loci. *Nat Genet* 50:928-936, 2018 [Erratum: *Nat Genet* 51:363, 2019]
45. Cybulski C, Górski B, Debniak T, et al: NBS1 is a prostate cancer susceptibility gene. *Cancer Res* 64:1215-1219, 2004
46. Leongamornlert DA, Saunders EJ, Wakerell S, et al: Germline DNA repair gene mutations in young-onset prostate cancer cases in the UK: Evidence for a more extensive genetic panel. *Eur Urol* 76:329-337, 2019
47. Rusak B, Kluźniak W, Wokołorczyk D, et al: Inherited NBN mutations and prostate cancer risk and survival. *Cancer Res Treat* 51:1180-1187, 2019
48. Wang Y, Dai B, Ye D: CHEK2 mutation and risk of prostate cancer: A systematic review and meta-analysis. *Int J Clin Exp Med* 8:15708-15715, 2015
49. Conti DV, Wang K, Sheng X, et al: Two novel susceptibility loci for prostate cancer in men of African ancestry. *J Natl Cancer Inst* 109:djx084, 2017
50. Southey MC, Goldgar DE, Winqvist R, et al: PALB2, CHEK2 and ATM rare variants and cancer risk: Data from COGS. *J Med Genet* 53:800-811, 2016
51. Pakkanen S, Wahlfors T, Siltanen S, et al: PALB2 variants in hereditary and unselected Finnish prostate cancer cases. *J Negat Results Biomed* 8:12, 2009
52. Mai PL, Best AF, Peters JA, et al: Risks of first and subsequent cancers among TP53 mutation carriers in the National Cancer Institute Li-Fraumeni syndrome cohort. *Cancer* 122:3673-3681, 2016
53. Amadou A, Achatz MIW, Hainaut P: Revisiting tumor patterns and penetrance in germline TP53 mutation carriers: Temporal phases of Li-Fraumeni syndrome. *Curr Opin Oncol* 30:23-29, 2018 [Erratum: *Curr Opin Oncol* 31:52, 2019]
54. Rana HQ, Gelman R, LaDuca H, et al: Differences in TP53 mutation carrier phenotypes emerge from panel-based testing. *J Natl Cancer Inst* 110:863-870, 2018
55. Robinson D, Van Allen EM, Wu YM, et al: Integrative clinical genomics of advanced prostate cancer. *Cell* 162:454, 2015
56. Annala M, Struss WJ, Warner EW, et al: Treatment outcomes and tumor loss of heterozygosity in germline DNA repair-deficient prostate cancer. *Eur Urol* 72:34-42, 2017
57. Giri VN, Obeid E, Gross L, et al: Inherited mutations in males undergoing multigene panel testing for prostate cancer: Emerging implications for personalized prostate cancer genetic evaluation. *JCO Precis Oncol* , 2017
58. Antonarakis ES, Lu C, Lubber B, et al: Germline DNA-repair gene mutations and outcomes in men with metastatic castration-resistant prostate cancer receiving first-line abiraterone and enzalutamide. *Eur Urol* 74:218-225, 2018
59. Mateo J, Cheng HH, Beltran H, et al: Clinical outcome of prostate cancer patients with germline DNA repair mutations: Retrospective analysis from an international study. *Eur Urol* 73:687-693, 2018
60. Giri VN, Hegarty SE, Hyatt C, et al: Germline genetic testing for inherited prostate cancer in practice: Implications for genetic testing, precision therapy, and cascade testing. *Prostate* 79:333-339, 2019
61. Nicolosi P, Ledet E, Yang S, et al: Prevalence of germline variants in prostate cancer and implications for current genetic testing guidelines. *JAMA Oncol* 5:523-528, 2019
62. Lang SH, Swift SL, White H, et al: A systematic review of the prevalence of DNA damage response gene mutations in prostate cancer. *Int J Oncol* 55:597-616, 2019
63. Schweizer MT, Antonarakis ES, Bismar TA, et al: Genomic characterization of prostatic ductal adenocarcinoma identifies a high prevalence of DNA repair gene mutations. *JCO Precis Oncol* , 2019

64. Isaacsson Velho P, Silberstein JL, Markowski MC, et al: Intraductal/ductal histology and lymphovascular invasion are associated with germline DNA-repair gene mutations in prostate cancer. *Prostate* 78:401-407, 2018
65. Pritchard CC: Molecular insights into the germline for prostate cancer initiation, progression, and aggressiveness. *Can J Urol* 26:24-26, 2019
66. Cheng HH: Germline contributions to metastatic prostate cancer. *Can J Urol* 26:19-21, 2019
67. AlDubayan SH: Considerations of multigene test findings among men with prostate cancer: Knowns and unknowns. *Can J Urol* 26:14-16, 2019
68. Giusti RM, Rutter JL, Duray PH, et al: A twofold increase in BRCA mutation related prostate cancer among Ashkenazi Israelis is not associated with distinctive histopathology. *J Med Genet* 40:787-792, 2003
69. Kirchoff T, Kauff ND, Mitra N, et al: BRCA mutations and risk of prostate cancer in Ashkenazi Jews. *Clin Cancer Res* 10:2918-2921, 2004
70. Agalliu I, Gern R, Leanza S, et al: Associations of high-grade prostate cancer with BRCA1 and BRCA2 founder mutations. *Clin Cancer Res* 15:1112-1120, 2009
71. Chandrasekar T, Gross L, Gomella LG, et al: Prevalence of suspected hereditary cancer syndromes and germline mutations among a diverse cohort of probands reporting a family history of prostate cancer: Toward informing cascade testing for men. *Eur Urol Oncol* [epub ahead of print on July 2, 2019]
72. Pettaway CA: African American and Asian males: What do we know about germline predisposition to prostate cancer. *Can J Urol* 26:27-28, 2019
73. Kwon DH, Borno HT, Cheng HH, et al: Ethnic disparities among men with prostate cancer undergoing GT. *Urol Oncol* 38:80.e1-80.e7, 2020
74. Momozawa Y, Iwasaki Y, Hirata M, et al: Germline pathogenic variants in 7,636 Japanese patients with prostate cancer and 12,366 controls. *J Natl Cancer Inst* 2019:djz124, 2019
75. Pilarski R: Current prostate cancer genetic testing capabilities and considerations. *Can J Urol* 26:38-39, 2019
76. Robson ME, Bradbury AR, Arun B, et al: American Society of Clinical Oncology policy statement update: Genetic and genomic testing for cancer susceptibility. *J Clin Oncol* 33:3660-3667, 2015
77. Al Olama AA, Kote-Jarai Z, Berndt SI, et al: A meta-analysis of 87,040 individuals identifies 23 new susceptibility loci for prostate cancer. *Nat Genet* 46:1103-1109, 2014
78. Benafif S, Kote-Jarai Z, Eeles RA: A review of prostate cancer genome-wide association studies (GWAS). *Cancer Epidemiol Biomarkers Prev* 27:845-857, 2018
79. Toland AE: Polygenic risk scores for prostate cancer: Testing considerations. *Can J Urol* 26:17-18, 2019
80. Seibert TM, Fan CC, Wang Y, et al: Polygenic hazard score to guide screening for aggressive prostate cancer: Development and validation in large scale cohorts. *BMJ* 360:j5757, 2018
81. Fritsche LG, Gruber SB, Wu Z, et al: Association of polygenic risk scores for multiple cancers in a phenome-wide study: Results from the Michigan Genomics Initiative. *Am J Hum Genet* 102:1048-1061, 2018
82. Riley BD, Culver JO, Skrzynia C, et al: Essential elements of genetic cancer risk assessment, counseling, and testing: Updated recommendations of the National Society of Genetic Counselors. *J Genet Couns* 21:151-161, 2012
83. Hampel H, Bennett R, Buchanan A, et al: A practice guideline from the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors: Referral indications for cancer predisposition assessment. *Genet Med* 17:70-87, 2015
84. Institute of Medicine (US) Committee on Assessing Genetic Risks; Andrews LB, Fullerton JE, et al (eds): *Assessing Genetic Risks: Implications for Health and Social Policy*. Washington, DC, National Academies Press, 1994
85. Stoll K, Kubendran S, Cohen SA: The past, present and future of service delivery in genetic counseling: Keeping up in the era of precision medicine. *Am J Med Genet C Semin Med Genet* 178:24-37, 2018
86. Patrick-Miller L, Egleston BL, Daly M, et al: Implementation and outcomes of telephone disclosure of clinical BRCA1/2 test results. *Patient Educ Couns* 93:413-419, 2013
87. Schwartz MD, Valdimarsdottir HB, Peshkin BN, et al: Randomized noninferiority trial of telephone versus in-person genetic counseling for hereditary breast and ovarian cancer. *J Clin Oncol* 32:618-626, 2014
88. Gray J, Brain K, Iredale R, et al: A pilot study of telegenetics. *J Telemed Telecare* 6:245-247, 2000
89. Hilgart JS, Hayward JA, Coles B, et al: Telegenetics: A systematic review of telemedicine in genetics services. *Genet Med* 14:765-776, 2012
90. Coelho JJ, Arnold A, Nayler J, et al: An assessment of the efficacy of cancer genetic counselling using real-time videoconferencing technology (telemedicine) compared to face-to-face consultations. *Eur J Cancer* 41:2257-2261, 2005
91. d'Agincourt-Canning L, McGillivray B, Panabaker K, et al: Evaluation of genetic counseling for hereditary cancer by videoconference in British Columbia. *BC Med J* 50:554-559, 2008
92. Trepanier AM, Allain DC: Models of service delivery for cancer genetic risk assessment and counseling. *J Genet Couns* 23:239-253, 2014
93. Buchanan AH, Rahm AK, Williams JL: Alternate service delivery models in cancer genetic counseling: A mini-review. *Front Oncol* 6:120, 2016
94. Mateo J, Carreira S, Sandhu S, et al: DNA-repair defects and olaparib in metastatic prostate cancer. *N Engl J Med* 373:1697-1708, 2015
95. Pomerantz MM, Spisák S, Jia L, et al: The association between germline BRCA2 variants and sensitivity to platinum-based chemotherapy among men with metastatic prostate cancer. *Cancer* 123:3532-3539, 2017
96. Abida W, Bryce AH, Vogelzang NJ, et al: Preliminary results from TRITON2: A phase 2 study of rucaparib in patients (Pts) with metastatic castration-resistant prostate cancer (mCRPC) associated with homologous recombination repair (HRR) gene alterations. *Ann Oncol* 29:viii271-viii302, 2018 (suppl 8)
97. Castro E, Romero-Laorden N, Del Pozo A, et al: PROREPAIR-B: A prospective cohort study of the impact of germline DNA repair mutations on the outcomes of patients with metastatic castration-resistant prostate cancer. *J Clin Oncol* 37:490-503, 2019
98. European Society for Medical Oncology: Olaparib outperforms enzalutamide or abiraterone acetate in men with mCRPC and HRR alterations. <https://www.esmo.org/oncology-news/olaparib-outperforms-enzalutamide-or-abiraterone-acetate-in-men-with-mcrpc-and-hrr-alterations>
99. Marshall CH, Sokolova AO, McNatty AL, et al: Differential response to olaparib treatment among men with metastatic castration-resistant prostate cancer harboring BRCA1 or BRCA2 versus ATM mutations. *Eur Urol* 76:452-458, 2019
100. Wu Y, Yu H, Zheng SL, et al: A comprehensive evaluation of CHEK2 germline mutations in men with prostate cancer. *Prostate* 78:607-615, 2018
101. Helfand BT, Xu J: GT for prostate cancer prognosis: Implications for AS. *Can J Urol* 26:48-49, 2019
102. Polascic TJ, Orabi H: Considerations of GT in prostate cancer early detection. *Can J Urol* 26:46-47, 2019
103. Hyatt C, Russo J, McDougall C: Genetic counseling perspective of engagement with urology and primary care. *Can J Urol* 26:52-53, 2019



AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**Implementation of Germline Testing for Prostate Cancer: Philadelphia Prostate Cancer Consensus Conference 2019**

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians ([Open Payments](#)).

Veda N. Giri

Stock and Other Ownership Interests: Novopyxis (I)

Karen E. Knudsen

Stock and Other Ownership Interests: Pfizer, Genomic Health

Honoraria: CellCentric, Sanofi

Consulting or Advisory Role: CellCentric, Sanofi, Atrin Pharmaceuticals, Context Therapeutics

Research Funding: Celgene

Travel, Accommodations, Expenses: Sanofi, Genentech

William K. Kelly

Honoraria: Janssen Oncology, Bayer

Consulting or Advisory Role: Merck Sharp & Dohme

Research Funding: Sanofi (Inst), Novartis (Inst), Janssen Oncology (Inst), Bayer (Inst), Exelixis (Inst), Seattle Genetics (Inst), Endocyte (Inst), Amgen (Inst), BioClin Therapeutics (Inst), Sarah Cannon Research Institute (Inst), F Hoffman-La Roche (Inst)

Travel, Accommodations, Expenses: Janssen Oncology, Merck Sharp & Dohme

Heather H. Cheng

Research Funding: Inovio Pharmaceuticals (Inst), Sanofi (Inst), Astellas Medivation (Inst), Janssen Oncology (Inst), Clovis Oncology (Inst), Color Foundation (Inst)

Kathleen A. Cooney

Patents, Royalties, Other Intellectual Property: Patent awarded for discovery of HOXB13 as prostate cancer susceptibility gene (Inst)

Travel, Accommodations, Expenses: Boston Scientific (I)

Michael S. Cookson

Honoraria: Merck, Janssen Biotech, Bayer, Astellas Pharma, Myovant Sciences

Consulting or Advisory Role: Merck, Janssen Biotech, MDxHealth, Bayer, Astellas Pharma, Myovant Sciences, TesoRx Pharma, Genomic Health, Ferring Pharmaceuticals, Precision Biopsy

Scott Weissman

Employment: Genome Medical

Stock and Other Ownership Interests: Genome Medical

Howard R. Soule

Leadership: WindMIL

Consulting or Advisory Role: Compugen, WindMIL

Travel, Accommodations, Expenses: Compugen, Sanofi, WindMIL

Daniel P. Petrylak

Stock and Other Ownership Interests: Bellicum Pharmaceuticals, TYME

Consulting or Advisory Role: Bayer, Exelixis, Pfizer, Roche, Astellas Pharma, AstraZeneca, Eli Lilly, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Clovis Oncology, Incyte, Janssen Oncology, Pharmacyclics, Seattle Genetics, Urogen Pharma, Advanced Accelerator Applications, Ipsen

Research Funding: Progenics (Inst), Sanofi (Inst), Endocyte (Inst), Genentech (Inst), Merck (Inst), Astellas Medivation (Inst), Novartis (Inst), AstraZeneca (Inst), Bayer (Inst), Eli Lilly (Inst), Innocrin Pharma (Inst), MedImmune (Inst), Pfizer (Inst), Roche (Inst), Seattle Genetics (Inst), Clovis Oncology (Inst), Bristol Myers Squibb (Inst), Advanced Accelerator Applications (Inst)

Expert Testimony: Celgene, Sanofi

Adam P. Dicker

Leadership: Department of Defense-Prostate Cancer Research Program, NRG Oncology, American Society for Radiation Oncology

Stock and Other Ownership Interests: Oncohost, Self Care Catalyst

Consulting or Advisory Role: EMD Serono, Janssen Oncology, Self Care Catalyst, Celldex, Johnson & Johnson, Roche, Apex, Cybrexa Therapeutics, Oncohost, Thirdbridge, Accordant

Research Funding: Prostate Cancer Foundation

Patents, Royalties, Other Intellectual Property: Recently filed patent "Doped BEO Compounds for Optically Stimulated Luminescence (OSL) and Thermoluminescence (TL) Radiation Dosimetry"

Expert Testimony: Wilson, Socini

Travel, Accommodations, Expenses: Merck, Ferring Pharmaceuticals, Self Care Catalyst, EMD Serono, Oncohost

Other Relationship: Dreamit Ventures

Uncompensated Relationships: Google

Colin C. Pritchard

Consulting or Advisory Role: Promega

Curtis A. Pettaway

Consulting or Advisory Role: Wolters-Kluwer

Research Funding: Beckmann-Coulter, MDxHealth

James L. Mohler

Patents, Royalties, Other Intellectual Property: Mohler JL, Fiandalo M, Watt D, Sviripa V: Compounds and methods to impair androgen receptor (AR) activation, impair dimerization, and/or impair AR transregulation. US provisional patent application 62/839,676, filed 4/27/2019, by Health Research & University of Kentucky Research Foundation (Inst); Mohler JL, Fiandalo M, Watt D, Sviripa V: Inhibitors of androgen receptor activation and methods of making and using same. US provisional patent application 62/890,292, filed 8/22/2019, by Health Research & University of Kentucky Research Foundation (Inst); Mohler JL, Fiandalo M, Watt D, Sviripa V: Spirocyclic dihydrotestosterone as ligand for proteolysis chimeras for AR degradation, imaging agents, and screening tools for the treatment of prostate cancer. US provisional patent application 62/844,062, filed 5/6/2019, by Health Research & University of Kentucky Research Foundation (revised; Inst)

J. Kellogg Parsons

Stock and Other Ownership Interests: Urigen, Pfizer, Johnson & Johnson, Omega Healthcare Investors

Honoraria: Sophiris Bio

Travel, Accommodations, Expenses: Sophiris Bio

Other Relationship: MDxHealth

Peter R. Carroll

Honoraria: Intuitive Surgical

Consulting or Advisory Role: Nutcracker Therapeutics

Amie Blanco

Employment: Biomarin (I)

Stock and Other Ownership Interests: Biomarin (I)

Ashley Woodson

Employment: Genome Medical

Travel, Accommodations, Expenses: Genome Medical

Mary-Ellen Taplin

Honoraria: Janssen-Ortho, Clovis Oncology, Astellas Pharma, Incyte, UpToDate, Research to Practice, Pfizer, Bayer, Amgen, AstraZeneca, Progenics, Guidepoint Global, Celegen, Merck

Consulting or Advisory Role: Janssen-Ortho, Bayer, Guidepoint Global, Best Doctors, UpToDate, Clovis Oncology, Research to Practice, Myovant Sciences, Incyte, Pfizer, AstraZeneca

Research Funding: Janssen-Ortho (Inst), Medivation (Inst), Bayer (Inst), Pfizer (Inst)

Travel, Accommodations, Expenses: Medivation, Janssen Oncology, Tokai Pharmaceuticals, Astellas Pharma, Incyte, Pfizer, Clovis Oncology, Bayer

Thomas J. Polascik

Honoraria: Endocare

Brian T. Helfand

Speakers' Bureau: Exact Sciences, Ambray Genetics

Colette Hyatt

Employment: GenomeSmart

Stock and Other Ownership Interests: GenomeSmart

Consulting or Advisory Role: GenomeSmart

Alicia K. Morgans

Honoraria: Genentech, Janssen Oncology, Sanofi, AstraZeneca, Astellas Scientific and Medical Affairs, Astellas Colombia, Janssen Oncology, Bayer

Consulting or Advisory Role: Genentech, AstraZeneca, Sanofi, Bayer, Astellas Pharma, Janssen Oncology

Research Funding: Bayer, Seattle Genetics, Astellas Pharma, Genentech, AstraZeneca

Travel, Accommodations, Expenses: Sanofi

Felix Feng**Leadership:** PFS Genomics**Stock and Other Ownership Interests:** PFS Genomics, Nutcracker Therapeutics, SerImmune**Honoraria:** Genentech**Consulting or Advisory Role:** Bayer, Blue Earth Diagnostics, Celgene, Medivation, Astellas Pharma, Sanofi, Genzyme, EMD Serono, Janssen Biotech
Research Funding: Zenith Epigenetics**Patents, Royalties, Other Intellectual Property:** Develop a molecular signature to predict radiation resistance in breast cancer, and this signature was patented by the University of Michigan; in the process of being licensed to PFS Genomics, a company that the author helped found (Inst)**Jacqueline Powers****Employment:** Carevive Systems**Honoraria:** CureConnect, Myriad Genetics**Consulting or Advisory Role:** Carevive Systems**Travel, Accommodations, Expenses:** Hospital of the University of Pennsylvania**Raoul Concepcion****Honoraria:** Clovis Oncology, InVita**Consulting or Advisory Role:** IntegraConnect**Speakers' Bureau:** Astellas Medivation, Janssen Oncology, Dendreon, Amgen**Daniel W. Lin****Consulting or Advisory Role:** Astellas Pharma, Clovis Oncology, Dendreon**Research Funding:** Genomic Health (Inst), GenomeDx (Inst), MDxHealth (Inst), Magforce**Anthony Costello****Honoraria:** Sandoz**Arthur L. Burnett****Honoraria:** Myriad Genetics, Novartis Pharmaceuticals, Futura Medical, Astellas Pharma, Boston Scientific (Inst)**Consulting or Advisory Role:** Myriad Genetics, Novartis Pharmaceuticals, Futura Medical, Astellas Pharma**Patents, Royalties, Other Intellectual Property:** Patents for the development of devices that may be used in pelvic surgeries, such as penile prosthesis implantation**Uncompensated Relationships:** Comphya, Reflexonic**Oliver Sartor****Stock and Other Ownership Interests:** Eli Lilly, GlaxoSmithKline, AbbVie, Cardinal Health, United Health Group, Varian Medical Systems, PSMA Therapeutics**Consulting or Advisory Role:** Bayer, Johnson & Johnson, Sanofi, AstraZeneca, Dendreon, Endocyte, Constellation Pharmaceuticals, Advanced Accelerator Applications, Pfizer, Bristol Myers Squibb, Bavarian Nordic, EMD Serono, Astellas Pharma, Progenics, Noxo, Blue Earth Diagnostics, Myovant, Myriad Genetics, Novartis, Clovis Oncology, Novartis**Research Funding:** Bayer (Inst), Johnson & Johnson (Inst), Sanofi (Inst), Endocyte (Inst), Innocrin Pharma (Inst), Merck (Inst), InVita (Inst), Constellation Pharmaceuticals (Inst), Advanced Accelerator Applications (Inst), AstraZeneca (Inst), Dendreon (Inst), SOTIO**Expert Testimony:** Sanofi**Travel, Accommodations, Expenses:** Bayer, Johnson & Johnson, Sanofi, AstraZeneca, Progenics**William B. Isaacs****Honoraria:** AstraZeneca**Travel, Accommodations, Expenses:** AstraZeneca**Jianfeng Xu****Patents, Royalties, Other Intellectual Property:** US9534256 B2: Methods and compositions for correlating genetic markers with risk of aggressive prostate cancer; US9534256 B2: Methods and compositions for correlating genetic markers with risk of aggressive prostate cancer; US9732389 B2: Methods and compositions for correlating genetic markers with prostate cancer risk; informal title: 33 SNPs for PCa risk**Jeffrey Weitzel****Speakers' Bureau:** AstraZeneca**Himisha Beltran****Consulting or Advisory Role:** Janssen Oncology, Genzyme, GlaxoSmithKline, AbbVie, Astellas Pharma, AstraZeneca, Pfizer**Research Funding:** Janssen Oncology (Inst), AbbVie (Inst), Stemcentrx (Inst), Eli Lilly (Inst)**Travel, Accommodations, Expenses:** Janssen Oncology**Alberto Briganti****Consulting or Advisory Role:** Astellas Pharma, Janssen-Cilag, OPKO Health, MDxHealth, Ferring Pharmaceuticals**Speakers' Bureau:** Astellas Pharma**Research Funding:** Sandoz-Novartis, Merck Sharp & Dohme**David Y. T. Chen****Stock and Other Ownership Interests:** Pfizer, Pfizer (I)**Robert B. Den****Employment:** Alpha TAU**Albert Dobi****Patents, Royalties, Other Intellectual Property:** Inventor of the ERG monoclonal antibody 9FY, licensed by the Biocare Medical; inventor of a urine biomarker panel, licensed by Exosome Diagnostics**E. David Crawford****Speakers' Bureau:** Bayer, Ferring Pharmaceuticals**James Eastham****Stock and Other Ownership Interests:** 3D Biopsy**Scott Eggener****Consulting or Advisory Role:** Sophiris Bio, Francis Medical, InSightec, Profound Medical**Speakers' Bureau:** Janssen Pharmaceuticals**Travel, Accommodations, Expenses:** Janssen Biotech, InSightec, Sophiris Bio
Uncompensated Relationships: Steba Biotech**Marc Garnick****Stock and Other Ownership Interests:** Immunogen, Exelixis, Dr. Consulta (Sao Paulo Brazil), Myovant**Consulting or Advisory Role:** Dr. Consulta (Sao Paulo Brazil), Eli Lilly, Amag, Steba Biotech, Agile Therapeutics, Janssen Oncology, Karyop**Expert Testimony:** Fitzpatrick Cella Harper and Scinto, US Department of Justice, Meyers ad Flowers**Nathan Handley****Research Funding:** Nektar Therapeutics (Inst)**Mark D. Hurwitz****Honoraria:** Pyrexar**Consulting or Advisory Role:** Neotherma**Speakers' Bureau:** Pyrexar**Patents, Royalties, Other Intellectual Property:** Provision patent holder for hyperthermia delivery system**R. Jeffrey Karnes****Patents, Royalties, Other Intellectual Property:** GenomeDx**Travel, Accommodations, Expenses:** GenomeDx**Lucia Languino****Stock and Other Ownership Interests:** Johnson & Johnson**Stacy Loeb****Stock and Other Ownership Interests:** Gilead Sciences (I)**Consulting or Advisory Role:** Bayer, Lumenis**Travel, Accommodations, Expenses:** Sanofi**Grace Lu-Yao****Employment:** Sun Pharma Advanced Research Company (I)**Leadership:** Sun Pharma Advanced Research Company (I)**Stock and Other Ownership Interests:** Merck (I)**Todd Morgan****Consulting or Advisory Role:** Myriad Genetics, TerumoBCT**Research Funding:** Myriad Genetics (Inst), MDxHealth (Inst), GenomeDx (Inst)**Jose Moreno****Stock and Other Ownership Interests:** Illumina, Invitae, ThermoFisher Scientific, Exact Sciences, Guardant Health, Bio-Techne**Research Funding:** Janssen Pharmaceuticals, Pfizer, Pillar Biosciences**Lorelei Mucci****Research Funding:** Sanofi (Inst), Astellas Pharma (Inst), Bayer (Inst), Janssen Pharmaceuticals (Inst)**Ronald E. Myers****Consulting or Advisory Role:** Exact Sciences**Sarah M. Nielsen****Employment:** Invitae**Stock and Other Ownership Interests:** Invitae**Consulting or Advisory Role:** AstraZeneca, Merck, Myriad Genetics**Speakers' Bureau:** AstraZeneca**Travel, Accommodations, Expenses:** Myriad Genetics, AstraZeneca, Invitae

Peter Pinto

Patents, Royalties, Other Intellectual Property: Royalties from US Patent No. 8948845: "System, methods, and instrumentation for image guided prostate treatment", with inventors/authors Brad Wood and Peter Pinto; the National Institutes of Health (NIH) and Philips (InVivo) have a licensing agreement. NIH does not endorse or recommend any commercial products, processes, or services. The views and personal opinions of authors expressed herein do not necessarily state or reflect those of the US Government, nor any official recommendation or opinion of the NIH or National Cancer Institute.

Wendy Poage

Employment: Servier

Stock and Other Ownership Interests: 3D Biopsy

Honoraria: Janssen Oncology, Myriad Genetics

Travel, Accommodations, Expenses: Pfizer, Dendreon, Janssen Oncology, Myriad Genetics

Ganesh V. Raj

Stock and Other Ownership Interests: EtiraRx,C-Diagnostics

Honoraria: Medivation, Janssen Biotech, Sanofi, Astellas Pharma

Consulting or Advisory Role: Pfizer, Bayer

Speakers' Bureau: Astellas Pharma

Research Funding: Janssen Biotech, Bayer

Patents, Royalties, Other Intellectual Property: Licensing

Timothy R. Rebbeck

Honoraria: AstraZeneca (I)

Consulting or Advisory Role: AstraZeneca (I)

Charles Ryan

Honoraria: Janssen Oncology, Bayer

Consulting or Advisory Role: Bayer, Dendreon, AAA

Research Funding: Clovis Oncology (Inst), Sanofi (Inst), Genzyme (Inst)

Howard Sandler

Stock and Other Ownership Interests: Radiogel

Consulting or Advisory Role: Janssen Pharmaceuticals

Other Relationship: Caribou Publishing

E. Michael D. Scott

Employment: Johnson & Johnson (I), Ex Archa, Calcium USA

Consulting or Advisory Role: Vavotar Life Sciences

Travel, Accommodations, Expenses: Vavotar Life Sciences

Other Relationship: International Myeloma Foundation, Prostate Cancer International

William Tester

Honoraria: DAVA Pharmaceuticals

Consulting or Advisory Role: Janssen Oncology

Edouard J. Trabulsi

Consulting or Advisory Role: GenomeDx

Speakers' Bureau: Johnson & Johnson, Janssen Oncology, Astellas Medivation, Pfizer

Neha Vapiwala

Consulting or Advisory Role: Magellan HealthRx

Evan Y. Yu

Consulting or Advisory Role: Janssen Oncology, Bayer, Merck, AstraZeneca, Amgen, QED, Dendreon, Seattle Genetics, Pharmacyclics, Clovis Oncology, Advanced Accelerator Applications, Sanofi, AbbVie, Myovant Sciences

Research Funding: Dendreon (Inst), Merck (Inst), Seattle Genetics (Inst), Daiichi Sankyo (Inst), Taiho Pharmaceutical (Inst), Pharmacyclics (Inst)

Leonard G. Gomella

Consulting or Advisory Role: Janssen Oncology, Astellas Pharma, Pfizer, Clovis Oncology, Bayer

Patents, Royalties, Other Intellectual Property: Patents held by Thomas Jefferson University

No other potential conflicts of interest were reported.

APPENDIX

TABLE A1. Priority Topics for Provider Education

Area of Knowledge	Percent Agreement
Recommend	
Purpose of genetic testing	100
Understanding types of results (mutation, VUS, negative)	92
Genetic Information Nondiscrimination Act and other laws that address discrimination	89
Hereditary cancer syndromes (HBOC, Lynch syndrome, HPC) that may be uncovered	86
Test options (focused prostate cancer panel v large cancer panel)	86
Additional cancer risks that may be uncovered	84
Potential out-of-pocket costs for genetic testing for patients	84
Privacy considerations of genetic tests	78
Cascade testing/additional familial testing/effect on family relationships	76
Consider	
Choice of laboratory for testing (pros and cons of test accuracy)	68
Data-sharing/data-selling policies of laboratories	62

NOTE. The Data Supplement provides educational resources for providers or trainees regarding germline testing. Abbreviations: HBOC, hereditary breast and ovarian cancer; HPC, hereditary prostate cancer; VUS, variant of uncertain significance.

TABLE A2. PCA Genetic Testing Implementation Barriers

Barrier	Percent Agreement
Recommend	
Increase advocacy and public awareness for PCA genetic testing and impact of genetic results for men and their families	99
Reimburse telehealth and telephone counseling	98
Implement virtual tumor boards, virtual molecular boards, or virtual genetics boards to disseminate genetics and molecular expertise	79
Redefine “actionability” to include familial impact of genetic testing for payer coverage	75
Consider	
Increase lobbying efforts to enhance payer coverage of PCA genetic testing	64
Engage primary care providers in genetic evaluation for PCA	63

Abbreviation: PCA, prostate cancer.

TABLE A3. Research Priorities to Advance PCA Genetics Knowledge and Practice

Priority Area	Percent Agreement
Recommend	
Genetics of PCA in diverse populations of men	93
Clinical outcomes by germline mutation status	93
Precision medicine trials	88
Precision PCA early detection trials	80
Basic science research into metastatic disease biology	76
Consider	
Implementation outcomes research regarding the alternate delivery of genetic counseling	72
Psychosocial outcomes of men undergoing genetic testing through various clinical approaches	63

Abbreviation: PCA, prostate cancer.