
Introduction to the 2019 Philadelphia Prostate Cancer Consensus Program: “Implementation of Genetic Testing for Inherited Prostate Cancer”

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In 2017 the Sidney Kimmel Cancer Center of Thomas Jefferson University held the first international consensus conference on the role of genetic testing for inherited

prostate cancer risk. This article outlines the key elements of our 2017 consensus meeting and discusses the rationale and design of our follow up 2019 Philadelphia Prostate Cancer Consensus titled the “Implementation of Genetic Testing for Inherited Prostate Cancer.”

Key Words: prostate cancer genetics, consensus conference

Prostate cancer continues to represent a major health care burden in the United States and in many other countries. Prostate cancer is recognized to be both a clinically and genetically heterogeneous disease with inherited factors accounting for significantly increased lifetime risk for the disease in certain men. Our understanding of the genetics of inherited prostate cancer is progressing rapidly. We are learning more about how these genetic results may inform all aspects of prostate cancer care from screening and diagnosis through the treatment of early stage disease to life threatening metastatic disease.

The carrier rates of germline mutations in men with metastatic prostate cancer has been reported at approximately 12%.¹ Additional studies from cohorts of men with prostate cancer have reported rates of germline mutations of 15%-17% regardless of stage.^{2,3} Genetic mutations in certain genes, such as *BRCA2*, significantly raise the lifetime risk for prostate cancer, and some are associated with risk for aggressive disease.^{4,5}

To add context to how rapidly this field is expanding we can refer to recent changes in the NCCN (National Comprehensive Cancer Network) guidelines (<https://www.nccn.org/professionals/physician>). Before 2017, detailed genetic testing guidelines for men with prostate cancer were only found in the NCCN Hereditary Breast and Ovarian Cancer (HBOC) guidelines.⁶ For many years this section of the NCCN guidelines had

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recommendations on how to approach prostate cancer screening in a male relative of a patient with HBOC. In 2016, the NCCN Prostate Cancer Detection Guidelines made the first mention of family history of *BRCA1/2* mutations in the context of prostate cancer screening (NCCN Guidelines Prostate Cancer Early Detection Version 1.2016). Since that time these prostate cancer guidelines have expanded and provided information on both early detection and treatment of localized and advanced prostate cancer in the setting of inherited mutations in genes such as *BRCA1*, *BRCA2* and other DNA repair gene alterations.^{7,8}

In order to bring some clarity and cohesiveness to this evolving area of genetic evaluation for inherited prostate cancer in 2017, we convened the first Philadelphia Prostate Cancer Consensus meeting. This meeting brought together a diverse multidisciplinary group to address a genetic evaluation framework for inherited prostate cancer in the multigene testing era. The panel members included over 70 stakeholders with expertise in prostate cancer early detection, treatment, genetic counseling, research, bioethics, as well as patient advocates and national organizations. The participants also included individuals with expertise in breast cancer and gynecologic oncology to provide perspectives on hereditary breast and ovarian cancer syndromes and models of genetic assessment.

The results of the 2017 consensus meeting were published in the *Journal of Clinical Oncology* in 2018.⁹ Some of the 2017 consensus findings included the following highlights and endorsements:

- Expansion of referral criteria to include age at diagnosis, broader family cancer history, and broader tumor sequencing results.
- Shared decision-making for genetic counseling and genetic testing for prostate cancer.
- Expansion of testing criteria to encompass hereditary cancer syndromes in which prostate cancer has been implicated.
- Genetic testing for men with metastatic castration-resistant prostate cancer.
- Expansion of genetic testing to include hereditary cancer syndromes or broader family cancer history.
- Expansion of *BRCA2*-informed prostate cancer screening to include consideration of age at diagnosis of prostate cancer in male blood relatives.
- Consideration of *HOXB13* genetic testing and the role in prostate cancer screening.
- Inclusion of genetic information in management discussions of early-stage and advanced prostate cancer.

- Consideration of the emerging role of *ATM* in prostate cancer management discussions.
- Articulation of needs for expanded research on the role of genetic testing in prostate cancer for African American men, outcomes, and cost of care.

Multigene panels are now widely available for testing for inherited prostate cancer from a variety of commercial and institutional laboratories. These include genes known to contribute to prostate cancer predisposition as well as increase the risk of other related cancers such as breast (both male and female), ovarian, pancreatic, melanoma, gastrointestinal (Lynch syndrome) and others. This expanded testing capability raises the importance of tailoring genetic counseling for males and their families regarding potential findings and implications to make informed decisions for proceeding with genetic testing.^{10,11} Furthermore, precision medicine in the advanced and metastatic setting and precision management in the early stage setting are now driving a significant portion of genetic testing from non-genetic practices^{12,13} such as oncology and urology, necessitating expert consensus regarding approaches for responsible implementation of genetic testing for men with prostate cancer.

The theme of our second consensus meeting is “Implementation of Genetic Testing for Inherited Prostate Cancer.” Critical issues to be addressed by the 2019 consensus include:

1. Update of genetic evaluation framework and genes associated with prostate cancer.
2. Delivery and incorporation of genetic testing and genetic counseling for men with all stages of prostate cancer from active surveillance through treatment of metastatic castration resistant prostate cancer for urologic and oncologic practices.
3. Delivery and incorporation of genetic testing and genetic counseling for prostate cancer screening and risk assessment.
4. Approaches for cascade testing for family members of male mutation carriers.
5. Optimum strategies for the education of urologic and oncologic providers.
6. Identification of gaps, such as application of genetic testing in diverse populations (e.g., African American, others) and defining the areas for future studies.

The consensus conference will be attended by a group of US and international experts spanning across disciplines involved in prostate cancer genetics including the following areas: urologists, medical oncologists and radiation oncologists involved with prostate cancer

diagnosis and treatment, genetic counseling, basic and clinical science research, policy experts, and patients and patient advocacy representatives. We invited members of various professional groups who are stakeholders in this area of integrating genetic testing and prostate cancer care. Members invited to attend the conference are from organizations such as several NCI-designated and community cancer centers, the National Comprehensive Cancer Network (NCCN), the National Cancer Institute (NCI), the American Society of Clinical Oncology (ASCO), the American Society for Therapeutic Radiation Oncology (ASTRO), the American Cancer Society (ACS), the American Urological Association (AUA), the Prostate Cancer Foundation (PCF), National Society of Genetic Counselors (NSGC), Prostate Cancer International (PCI), the Prostate Conditions Education Council (PCEC), the Society of Urologic Oncology (SUO), patient advocates and other groups. Key organizations will be provided with the final consensus document as recommended by the steering committee and given the opportunity to endorse the final consensus statements prior to submission and publication. Steering Committee members are listed in Table 1.

Expert speakers were invited by the program leadership based on their expertise in this area to present information to help address the overarching consensus questions. A multidisciplinary steering committee reviewed and approved the program content.

Beginning on October 4, 2019, the consensus meeting will be conducted in a similar structure and design of the modified Delphi method as our first meeting held in Philadelphia in March 2017. A series of speakers will address different aspects of this year's theme of "implementation of genetic testing for prostate cancer". The final session on Saturday, October 5 will involve the participants answering a series of questions informing the best practice approach to prostate cancer genetic testing. An audience response system will be used to capture the audience responses to a series of these critical questions. After the information is gathered a final consensus manuscript will be drafted to address the questions and will be circulated to the group for final comment and approval prior to submission for publication. The choice of the journal will be selected by the conference leadership and steering committee.

TABLE 1. "Implementation of Genetic Testing for Inherited Prostate Cancer" 2019 Philadelphia Prostate Cancer Consensus steering committee members.

Chair: Dr. W. Kevin Kelly – Sidney Kimmel Cancer Center at Jefferson, Philadelphia, PA
Dr. Michael S. Cookson – President Elect Society of Urologic Oncology (SUO). University of Oklahoma, Oklahoma City, OK
Dr. William L. Dahut – National Cancer Institute, Bethesda, MD
Dr. Adam P. Dicker – Sidney Kimmel Cancer Center at Jefferson, Philadelphia, PA
Dr. Felix Feng – UCLA San Francisco, CA
Dr. Veda N. Giri – Sidney Kimmel Cancer Center at Jefferson, Philadelphia, PA
Dr. Leonard G. Gomella – Sidney Kimmel Cancer Center at Jefferson, Philadelphia, PA
Dr. Karen E. Knudsen – Sidney Kimmel Cancer Center at Jefferson, Philadelphia, PA
Dr. Daniel W. Lin – University of Washington, Fred Hutchinson Cancer Research Center, Seattle, WA
Dr. Stephen C. Peiper – Sidney Kimmel Cancer Center at Jefferson, Philadelphia, PA
Dr. Daniel P. Petrylak – Yale Cancer Center, New Haven, CT
Mr. Robert Pilarski – Ohio State University, Columbus, OH
Ms. Wendy L. Poage – Executive Director Prostate Conditions Education Council (PCEC), Denver, CO
Mr. Michael D. Scott – Prostate Cancer International (PCI), Philadelphia, PA
Dr. Howard R. Soule – Prostate Cancer Foundation (PCF) Santa Monica, CA
Mr. Scott Weissman – National Society of Genetic Counselors, Chicago, IL
Dr. Richard Wender – American Cancer Society, Atlanta, GA

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This second 2019 Philadelphia Prostate Cancer Consensus is being made possible by support from Jefferson’s Sidney Kimmel Cancer Center (<http://www.kimmeltcancercenter.org>), Jefferson’s Department of Urology and through grants from a variety of pharmaceutical, reference laboratories, and other interested parties. Without their financial support this meeting would not be possible. Industry sponsors have the option for their representatives to attend the lectures and discussions as non-voting observers. The meeting was developed as a non-CME certified meeting. Current sponsorship is acknowledged elsewhere in this supplement.

This October 2019 supplement of *The Canadian Journal of Urology International* contains summaries of the 2019 consensus presentations. It is not meant to be a substitute for the final consensus document. Rather it provides a high-level overview of the information that will be used in the consensus panel discussions for the creation of the final consensus statements. It also provides consensus speakers, moderators and participants with pre-meeting review materials to enhance their participation. We hope that the information published herein will also be useful to a broader audience who are not participating in our consensus but are interested in this rapidly evolving field.

Disclosures

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- Mitra A, Fisher C, Foster CS et al. Prostate cancer in male BRCA1 and BRCA2 pathogenic variant carriers has a more aggressive phenotype. *Br J Cancer* 2008;98(2):502-507.
- Na R, Zheng SL, Han M et al. Germline pathogenic variants in ATM and BRCA1/2 distinguish risk for lethal and indolent prostate cancer and are associated with early age at death. *Eur Urol* 2017;71(5):740-747.
- Gomella LG. Prostate, breast and ovarian cancer genetic risk assessment: connecting the dots. *Can J Urol* 2016;23(5):8429.
- https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf (accessed August 18, 2019)
- https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf (accessed August 18, 2019)
- 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* 2018;36(4):414-424.
- Hall MJ, Forman AD, Pilarski R et al. Gene panel testing for inherited cancer risk. *J Natl Compr Canc Netw* 2014;12(9):1339-1346.
- Robson ME, Bradbury A, Arun B et al. American Society of Clinical Oncology policy statement update: genetic and genomic testing for cancer susceptibility. *J Clin Oncol* 2015;33(31):3660-3667.
- Cheng HH, Sokolova AO, Schaeffer EM et al. Germline and somatic mutations in prostate cancer for the clinician. *J Natl Compr Canc Netw* 2019;17(5):515-521.
- Giri VN, Hyatt C, Gomella LG. Germline testing for men with prostate cancer: navigating an expanding new world of genetic evaluation for precision therapy and precision management. *J Clin Oncol* 2019;37(17):1455-1459.

References

- Pritchard CC, Mateo J, Walsh MF et al. Inherited DNA-repair gene pathogenic variants in men with metastatic prostate cancer. *N Engl J Med* 2016;375(5):443-453.
- 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* 2019;79(4):333-339.
- Nicolosi P, Ledet E, Yang S, Prevalence of germline variants in prostate cancer and implications for current genetic testing guidelines. *JAMA Oncol* 2019;5(4):523-528.