REVIEW

Philadelphia Prostate Cancer Genetic Consensus Conference 2019 and implications for military medicine

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Introduction: *The objective of our review is to summarize the 2019 Philadelphia Prostate Cancer Genetic Consensus recommendations and discuss their implications to the US Military Health System.*

Materials and methods: *Literature review.*

Results: *Our fighting force and retired service members will significantly benefit from the Philadelphia Prostate Cancer Genetic Consensus recommendations. Moreover, the experience of the equal access US Military Health System may help advancing genetic testing for cancer at national levels.*

Conclusions: *Priorities recommended by the 2019 Consensus for more research on genetic predisposition to prostate cancer in racially diverse populations is a promising step. The US Military Health System has the ability of providing equal access to implement advanced germline testing for its racially diverse population.*

Key Words: prostate cancer, genetic testing, Military Healthcare System, cancer genomics

Introduction

In 2017, a multidisciplinary panel of experts in prostate cancer met in Philadelphia to establish a consensus statement to "address a genetic evaluation framework for inherited prostate cancer in the multigene testing era," as genetic testing became more widely available and less expensive".[1] The panel focused on the following questions: (1) Who should undergo genetic counseling and genetic testing for PCa? (2) Which genes should be tested based on clinical and/or familial scenarios? (3) How should genetic test results inform prostate cancer screening? (4) Should genetic test results inform management of early-stage/localized prostate cancer, advanced/high-risk prostate cancer, and metastatic castration-resistant prostate cancer (mCRPC)? The conference was organized such that panel participants were invited and sent literature for review prior to the conference. During the conference, evidence was presented, and the panelists discussed questions in open debate. Following deliberation, the panelists voted anonymously and produced consensus guidelines.

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Since 2017, commercially available genetic testing has proliferated with increasing information on target genes, expanded guidelines for genetic testing for prostate cancer, and greater need for genetic counseling. The 2019 Consensus Conference met October 4-5, 2019, in Philadelphia to address new emerging challenges and gaps in prostate cancer genetic testing guidelines.[2] The conference consisted of a 97-member multidisciplinary panel, including patient advocates, urologists, medical oncologists, radiation oncologists, clinical geneticists, genetic counselors, primary care providers pathologists, and researchers in the implementation, population, epidemiological, and basic sciences. The 2019 Consensus was focused on testing indications, genes, and management guidance that were vastly expanded due to increased scientific insights and new treatment options since 2017. Major topics for consensus included which men to test, appropriate pretest counseling or informed consent, optimal genes to test, how genetic results may inform management or screening across the stage and risk spectrum, and post-test disclosure elements.[2] In addition, the 2019 conference included the powerful voice of patient advocates in the entire spectrum of discussions, as well as debate on the growth of genetic testing options, including multigene panels and polygenic risk scores, and the shortage of genetic counselors with attention to alternate genetic counseling delivery models. For each question proposed to the panelists, recommendations were made with either strong consensus in voting (≥ 75% agreement with answer choice) or moderate consensus (50%-74% agreement). Criteria that achieved strong consensus were designated as "Recommend" and those with moderate consensus were designated as "Consider" in the final framework.

Philadelphia Prostate Cancer Genetic Consensus Conference 2019 recommendations

The 2019 Consensus recommendations for testing indications, genes to evaluate, and management of findings, were largely based on the burden of disease: metastatic, non-metastatic, and unaffected males with positive family history. For metastatic prostate cancer, germline testing guidelines were established with the goals of informing therapeutic decision-making, clinical trial eligibility, and identification of hereditary cancer syndrome. The 2019 Consensus recommends germline testing for all metastatic prostate cancer (Consensus: Strong). The 2019 Consensus also recommends specific genes to test in patients with metastatic prostate cancer to guide therapeutic decision-making. Testing for *BRCA1/2* in males with metastatic prostate cancer is recommended to inform the response to poly (ADP) ribose polymerase (PARP) inhibitors (Consensus: Strong for *BRCA2*, Moderate for *BRCA1*) and platinum-based therapies (Consensus: Moderate for *BRCA2*, Moderate for *BRCA1*).[3-6] The 2019 Consensus endorsed testing for *ATM* in metastatic prostate cancer (Consensus: Moderate) since *ATM* has the second highest germline mutation rates in metastatic prostate cancer.[7-11]

DNA mismatch repair (MMR) genes: *MSH2* and *MSH6* (Consensus: Strong) and *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM* (Consensus: Moderate) were also included in the genes recommended to be tested for metastatic prostate cancer. Testing for DNA MMR mutations in metastatic prostate cancer is driven by new insights in treatment response. The 2019 Consensus recommends with moderate consensus DNA MMR mutation status to inform response to anti-programmed death-1 (PD-1) therapy.[12] The 2019 Consensus also recommends (Consensus: Moderate) the initiation of PARP inhibitor therapy, rather than taxane, in men with DNA repair gene mutations after progression on abiraterone.[4,5] There was strong consensus for germline testing in men with metastatic prostate cancer to enroll in precision medicine trials due to the significant expansion of genetically-informed clinical trials in metastatic prostate cancer.[13] A comprehensive gene panel testing may be considered for therapy or clinical trial eligibility for genes including *BRCA2*, *BRCA1*, *ATM*, *CHEK2*, *PALB2*, *RAD51D*, *NBN*, *MLH1*, *MSH2*, *PMS2*, and *MSH6*.[14] Somatic next-generation sequencing (NGS) was also recommended for all men with metastatic prostate cancer (Consensus: Strong), as well as confirmatory germline testing for the following somatic mutations: *BRCA2* (Consensus: Strong), *BRCA1*, *MSH2*, *MSH6*, *ATM* (Consensus: Moderate), and for additional genes based on personal or family history (Consensus: Strong). The 2019 Consensus also recommends reflex testing (Consensus: Moderate).

For non-metastatic prostate cancer, guidelines were established with the goals of identifying hereditary cancer syndrome and guiding active surveillance discussions. The 2019 Consensus expands genetic testing in non-metastatic prostate cancer on positive family history as well as new insights on convincing associations with hereditary cancer syndromes. The 2019 Consensus recommends genetic testing in non-metastatic prostate cancer in males with ≥ 1 of the following: Ashkenazi Jewish ancestry (Consensus: Moderate) due to its association with HPC and HBOC,[15-17] MSH2 loss on tumor

immunohistochemistry (Consensus: Moderate) due to its association with Lynch Syndrome,[18,19] intraductal pathology (Consensus: Moderate), also associated with Lynch Syndrome,[20,21] and advanced disease: T3a or higher (Consensus: Moderate) or Grade Group 4 (Gleason 8) or above (Consensus: Moderate).[22]

The other goal of the 2019 Consensus for germline testing in non-metastatic prostate cancer was to inform active surveillance discussions, which typically entails a prostate-specific antigen (PSA) blood test approximately every 6 months, a digital rectal exam (DRE) at least once a year, and prostate biopsies and imaging tests every 1 to 3 years. Testing for *BRCA2* (Consensus: Strong) and *ATM* (Consensus: Strong) was recommended based association of more aggressive disease with *BRCA2* and *ATM* mutations.[7,8,16,23-32] Additional genes could be tested based on personal or family history (Consensus: Moderate).

The 2019 Consensus also made recommendation for genetic testing in unaffected males with family history considerations with the goals of identifying hereditary cancer syndrome and informing prostate cancer screening discussions. Prostate family history criteria for genetic testing include ≥ 1 first-degree relative (father, brother, or son) or ≥ 2 male relatives with ≥ 1 of the following: prostate cancer diagnosis < 60 years old, death from prostate cancer, and metastatic prostate cancer (Consensus: Strong). Family history criteria of other cancers include ≥ 2 family members with cancers part of the Hereditary Breast and Ovarian Cancer or Lynch Syndrome spectra. In patients meeting family history criteria, the 2019 Consensus recommends testing for the following genes found to have increased risk of the development and aggressiveness of prostate cancer: *BRCA1* (Consensus: Strong), *BRCA2* (Consensus: Moderate), DNA MMR genes (Consensus: Moderate), and *HOXB13* (Consensus: Strong).[16,23-31,33-39]

Inconsistencies in NCCN guidelines also drove the 2019 Consensus to establish an agreement on patients' age at which to begin screening for prostate cancer in men at increased risk. In the NCCN Genetic/Familial High-Risk Assessment: Breast and Ovary (Version 3.19), prostate cancer screening was recommended to begin at age 45 in known *BRCA1/2* carriers, whereas the NCCN Prostate Cancer Early Detection (Version 4.19) guidelines recommended testing start at age 40 in known *BRCA1/2* carriers.[22,40] The 2019 Consensus chose the younger of the ages (40 years old) or 10 years prior to age at diagnosis of a family member to start screening and recommended screening in unaffected males with *BRCA2* (Consensus: Strong) and *BRCA1*, *HOXB13*, *ATM*, and DNA MMR mutations (Consensus: Moderate). The 2019 Consensus also endorses with strong consensus referral of unaffected male mutation carriers to specialty prostate cancer high risk clinics and enrollment in prostate cancer screening trials.

Prostate cancer genetic testing capabilities and considerations

The panel also discussed multigene panel testing considerations. The 2019 Consensus highlighted 10 genetic testing laboratories offering multigene panels specifically for prostate cancer genetic testing. The capabilities and limitations of the various multigene panels were thoroughly discussed. Among these labs, there was large variation in the specific genes and the numbers of genes tested, ranging from five to 16.[2] Smaller panels were found to be more specific to prostate cancer and based on guidelines but may not include relevant genes or fully assess specific genes for mutations, potentially missing pathogenic or targetable mutations. Conversely, the larger panels may identify gene mutations not related to prostate cancer and reveal unforeseen cancer risks to address to men and their families. Furthermore, with a greater number of genes tested by these multigene panels, there is a higher risk of uncovering variants of unknown significance.[41-44] Due to the significant variation among labs conducting multigene panel testing for prostate cancer, the 2019 Consensus did not endorse multigene panels from specific labs but, rather, was explicit in recommending specific genes to test.

Genetic counseling

The 2019 Consensus addressed the critical shortage of genetic counseling in the face of the rising demand for prostate cancer genetic testing. This has forced providers not formally trained in genetic counseling such as oncologists, urologists, and primary care providers to order prostate cancer genetic testing and to offer counseling. While these providers may understand the genes and their therapeutic and screening implications, the complexities of genetic counseling (cancer inheritance, unforeseen additional cancer risks, impact of the results on family, genetic discrimination laws, and the interpretation of the results) and the time required to properly offer this counseling often exceeds the capabilities of these non-genetic providers. The 2019 Consensus explored alternative options in the delivery of critical information. There was strong consensus that practices should consider multiple models to address patients' needs (Consensus: Strong). Prioritization of collaborative models included:

(1) point-of-care model with limited pretest family collection, (2) point-of-care model with full pretest family history collection, and (3) traditional model with upfront referral to genetic counselor. The 2019 Consensus also recommends with strong consensus utilizing technology to deliver this information: videos to deliver pretest informed consent and telehealth or telephone delivery of genetic counseling as a suitable alternative to an in-person visit. Alternate genetics practice models were also reviewed, such as counseling aids, group counseling, and use of genetic extenders, though patient outcomes data in a male population are needed. The point-of-care/hybrid models, in which a non-genetic provider performs pretest informed consent and orders genetic testing, with handoff to a genetic counselor/specialist after test results return, were discussed in comparison with the traditional genetic counseling model. Recommendations from the 2019 on genetic counseling models provide guidance to address the challenge of integrating genetic testing into oncology and urology clinical workflows.[45]

Discussion

Implications of 2019 Consensus recommendations to Military Health System

Prostate cancer is an area of interest for the U.S military. As of 2018, 83.5% of the active duty population are men.[46] According to the Defense Health Agency (DHA) Medical Surveillance Monthly Report (MSMR), 1,046 active duty servicemembers were diagnosed with prostate cancer between 2005 and 2014, consisting of 11.7% of the total cancer diagnoses.[47] Similarly elevated rates of prostate cancer are observed in African Americans , who make up 17.1% of US active duty servicemembers,[46] compared to 13.4% of the overall US population.[48] The 2019 Consensus guidelines have major implications to the Military Health System (MHS) with its comprehensive care in expanding genetic testing in men with prostate cancer.

The MHS is a unique entity among US healthcare systems in which comprehensive care is provided to active duty servicemembers and their family members as well as retirees at no cost. As equal access system, patients within the MHS do not face the obstacle of insurance payer coverage, a major concern among the 2019 Consensus in implementing prostate cancer genetic testing, and all patients have equal access to screening, treatment, and follow up. The expanded testing guidelines from 2019 Consensus allow the MHS to test a larger cohort of patients and can guide clinicians in management decisions from treatment options to active surveillance and screening.

The MHS now regularly offers genetic testing in a variety of settings. For men with strong family history of prostate cancer, and those with oncologic family history concerning for Lynch Syndrome, genetic counseling is offered, and testing is made available to inform screening interval recommendations and counseling. For men with screen-detected prostate cancer, genetic testing is commonly used to guide decisions to proceed with active surveillance or with local treatment. All men with metastatic prostate cancer undergo genetic testing in order to guide treatments. Men presenting to the MHS from other health systems, such as the VA, are offered testing upon enrollment with the MHS. Multidisciplinary prostate clinics, among first from the beginning, are designed within the MHS to allow for urologic oncology, medical oncology, radiation, oncology, social work, sexual medicine, and genetics counselors to work together with patients in each stage of prostate cancer diagnosis and treatment.

The MHS is also adapting to the nationwide shortage of genetic counselors. The 2019 Consensus recommends utilization of telemedicine for genetic counseling, something the MHS is already conducting. Due to the wide geographic distribution of the many MTFs nationwide, it is not currently possible to provide access to a genetic counselor at every MTF. In 2017, the MHS developed a pilot program that utilized clinical geneticists at two MTFs to provide genetic services to military bases within and outside of the continental United States. The MHS hopes to develop a centralized core of clinical geneticists and genetic counselors to remotely service the entire MHS when an in-person genetic counselor is unavailable.[49]

Future directions of prostate cancer genetic testing from 2019 Consensus

The 2019 Consensus meeting offers a landmark step in assisting urologists, oncologists, and genetic counselors in the ever-changing landscape of genetic testing for prostate cancera. In addition to making recommendations for patients and genes to test and how results may inform treatment options, the panel also identified areas in need of further research. Among these needs is a further understanding of prostate cancer genetics in racially diverse populations. The 2019 Consensus guidelines make no specific recommendations to various races or ethnicities, other than Ashkenazi Jews. This inclusion in the 2019 Consensus can be attributed to how well-studied the Ashkenazi Jewish population is, but it also highlights the lack of research in prostate cancer genetics in other populations, particularly African American men.

The African-American population has the highest rates of prostate cancer (1.4 times higher risk of being diagnosed than Caucasian males), and a mortality rate of 43 per 100,000 in the period 2008-2011, compared to whites (19.8 per 100,000), Hispanics (17.8 per 100,000) and Asian/Pacific Islanders (9.4 per 100,000).[50,51] The National Cancer Institute reported similar numbers: lifetime risk of prostate cancer death was 4.2% for African American men, 2.9% for Hispanic men, 2.3% for white men, and 2.1% for Asian and Pacific Islander men.[52] These disparities were attributed to socioeconomic factors such as barriers to healthcare access leading to more advanced disease at presentation, different treatment options, and worse disease surveillance.[50] However, after adjusting for the effects of socioeconomic factors, racial disparities in prostate cancer incidence and mortality rates remain significant, suggesting a greater contribution from molecular and genetic factors.[53] Furthermore, a March 2019 report to the US House and Senate Armed Services Committees demonstrated comparable prostate cancer rates, morbidity, and mortality in African American active duty servicemembers to African Americans in the general population despite no racial disparities related to screening, treatment, and risk assessment in the equal access MHS, yet suggesting a genetic component.[54] Tan et al summarizes the recent advances in prostate cancer genomics is the African American population and its underrepresentation in the study of genetics of prostate cancer, including high risk loci in chromosome 8p24.[55]

While current literature acknowledges the presence of genetic and cancer genomic differences in prostate cancer of African Americans, the differences are yet to be translated to broadly applicable assays. The lack of inclusion of specific recommendations for African Americans in the 2019 Consensus is reflective of the need for more translational research. A very progressive move of the attendees of the 2019 conference was to spotlight issues regarding racial differences in prostate cancer genetics (and all genomics) that were debated at great intensity. It is foreseeable that a strong consensus will be reached on follow up meetings focusing on aspects of prostate cancer genetic testing of African American men. The current panel achieved strong consensus that African American males should follow the same criteria as males of other race groups until additional genetic data in African American males are available (Consensus: Strong).

Lack of research on racially diverse populations is in part due to the low enrollment of African Americans in studies on prostate cancer genomics. Oh et al showed total representation across multiple studies of minority populations has been low, with African Americans accounting for 6% across study cohorts.[56] Similarly, the PLCO trial, a major trial on prostate cancer screening published in the *New England Journal of Medicine*, enrolled 4% African American men, which was not enough to determine whether the overall trial results differed for African American men.[57] Underrepresentation of African-Americans in studies of prostate cancer germline testing may also contribute to higher rates of variants of unknown significance (VUS) relative to Caucasian and Ashkenazi Jewish men.[58] Strong emphasis on the need for more research in diverse populations by the 2019 Consensus may lead to greater enrollment of African American participants in genetic studies and ultimately to the development of new treatment options.[59]

Indeed, the increased rates of prostate cancer in African Americans are of national levels of concerns; however, it poses particular concerns in the MHS with high representation of African American fighting force and retirees and high rates of prostate cancer among this population. African Americans make up 17.1% of US active duty servicemembers,[46] compared to 13.4% of the overall US population.[48] Multiple studies have found elevated rates of prostate cancer in African American active-duty servicemembers. In 2009, Zhu et al compared prostate cancer incidence between the military population and general population from 1990 to 2004, using age-adjusted incidence rates to control for the effects of different age distributions between the two populations.[60] The study found that the age-adjusted incidence rates of prostate cancer rates in African Americans serving in the military were higher than those in the general population. A 2019 Report to House and Senate Armed Services Committees found among active duty servicemembers, African Americans had more than two-fold greater incidence of prostate cancer diagnosis compared to Caucasian counterparts.

The MHS possesses the access to care resources to focus on researching germline testing in racially diverse populations and further the scientific field's understanding of prostate cancer genomics among African Americans. The MHS has already shown mitigation of socioeconomic barriers to care for African Americans in prostate cancer screening and treatment and other entities. The 2019 Report to House and Senate Armed Services Committees on prostate cancer among active duty servicemembers found African American men were 1.67 times as likely to receive any screening or risk assessment, were 1.25 times more likely than Caucasians to receive any treatment, and had similar or higher rates of every type of procedure related to

treatment, including prostatectomy, brachytherapy, external beam radiation therapy, and hormonal therapy.[54] Several other studies have also shown minimization of socioeconomic barriers and racial disparities within the MHS. Changoor et al studied screening rates for colorectal cancer in 29,944 patients in the MHS between 2007-2010. Compared with Caucasians, African American patients, who made up 20.3% of the cohort, had higher screening rates (56.5% vs. 53.5% among Caucasians) and had 20% higher risk-adjusted odds of being screened.[61] In a study of over 87,000 patients treated for traumatic injuries within the MHS, Chaudhary et al found decreased odds of 90-day complications and lesser odds of readmission in 30 days for African Americans.[62] Zogg et al reviewed over 101,000 patients who underwent emergency general surgery, finding lack of worse mortality and readmission outcomes among minority patients at 30, 90, and 180 days.[63] The same, effective strategies that have minimized worse healthcare outcomes and eliminated barriers to screening and treatment for prostate cancer and other cancers in the African American population within the MHS may be utilized to implement germline testing based on the 2019 Consensus recommendations. Furthermore, the full coverage provided at no cost to patient within the MHS eliminates another obstacle for implementing prostate cancer genetic testing that the 2019 consensus address, insurance payer coverage.

Thus, the MHS' ability to implement germline testing based on the 2019 Consensus recommendations may provide a larger and more racially diverse cohort in future research on prostate cancer genetics and genomics.

In addition to the MHS' ability to apply the 2019 Consensus expanded testing recommendation and increase genetic testing in racially diverse, its capabilities and prioritization of prostate cancer research uniquely position the MHS in this field with forthcoming impact on national level of discussions, particularly, in furthering our understanding of prostate cancer genetics and genomics in racially diverse populations. The Prostate Cancer Research Program under the U.S. Army Medical Research and Materiel Command established a strategic plan in 2018 with a goal to "reduce lethal prostate cancer in African Americans, veterans, and other high-risk populations."[64] This has led to numerous ongoing projects focused on prostate cancer health disparities and prioritizes funding for research on the underlying factors that contribute to racial disparities. As the 2019 Consensus calls for more focus on prostate cancer genetics in African Americans, the MHS is already conducting such research.

The Center for Prostate Cancer Research (CPDR), the John P. Murtha Cancer Center, the Uniformed Services University of Health Sciences, and the Walter Reed National Military Medical Center have made multiple recent contributions addressing the disparity in incidence, mortality, and understanding of genetics of prostate cancer in racial and ethnic minorities. Petrovics et al conducted sequencing of *BRCA1* and *BRCA2* genes (Ion AmpliSeq targeted sequencing) from archived blood DNA specimens in 1240 prostate cancer patients, including 30% African American patients, demonstrating increased rates of *BRCA1/2* VUS in African Americans compared to Caucasian Americans (4.6 vs. 1.6%, respectively).[65] For the first time, the frequencies of somatic cancer drivers were shown to be different between prostate cancer of African and Caucasian American men in the MHS, a system that minimizes socioeconomic differences and access to health care. Tan et al reviewed the recent progress of prostate cancer genetics in minority populations as increased efforts sequencing larger numbers of tumor specimens from more diverse populations have discovered distinct genomic alterations.[55] In another study conducted by Petrovics et al, somatic deletion on chromosome 3q13.31 centering on the LSAMP locus was found to be prevalent in tumors from African American men. These deletions were associated with more rapid disease progression. Conversely, African Americans demonstrated significantly lower rates of *PTEN* and *ERG* alterations, common driver mutations, compared to Caucasian men.[66]

The MHS has made significant efforts over the past decade to integrate genomic medicine into everyday healthcare of service members and their families. The MHS has its own reference molecular diagnostic laboratory, the Air Force Medical Genetics Center (AFMGC) at Keesler Medical Center, Keesler Air Force Base, in Biloxi, Mississippi, with capabilities in prenatal diagnosis, cytogenetic laboratory services, molecular and clinical genetics, and genetics education.[49] Founded in 1979, the lab serves multiple military treatment facilities (MTFs) within the MHS. The MHS, fostered by Precision Medicine Initiative and the Cancer Moonshot in 2016, has also developed partnerships with multiple major civilian institutions including the MilSeq and APOLLO projects. The MilSeq project, in collaboration Harvard Medical School and the Baylor School of Medicine seeks to answer questions regarding the integration of genomic medicine into the day-to-day practice of medicine. The MHS is also participating in the Applied Proteogenomics OrganizationaL Learning and Outcomes (APOLLO) with the National Cancer Institute and Veterans Affairs to utilize genomic and

proteogenomic data in cancer patients to inform personalized treatment options. The Murtha Cancer Center at Walter Reed Military Medical Center contributes biobanking of specimens to be analyzed at The American Genome Center (TAGC), a high throughput genome sequencing center at the Uniformed Services University of the Health Sciences (USU). TAGC provides core support for genome sequencing, RNA sequencing, and expert bioinformatics analysis to researchers across the MHS. Such capabilities, particularly from TAGC and AFMGC, may be utilized to better understand germline mutations in racially diverse populations within the MHS.

The 2019 Consensus emphasized attention to cascade testing in families in improving the understanding of prostate cancer genetics in African Americans. Cascade testing poses logistic challenges in collecting samples from multiple family members, who may be geographically separated, have different health insurance coverage, or be deceased. The Department of Defense Serum Repository (DODSR) may facilitate cascade testing for multiple family members, if these family members served in the military where sequential serum samples are marked for cancer studies. The DODSR holds over 60 million serum specimens for more than 10 million servicemembers since 1990, which were collected after routine HIV antibody testing and before and after major deployments and are accompanied by the servicemember's electronic health records. Lee et al have utilized the DODSR to identify serum protein biomarkers for detection of oropharyngeal squamous cell carcinoma (OPSCC). Researchers retrieved serum samples drawn 2 and 4 years prior to OPSCC diagnosis that were stored in the DODSR and compared them with samples drawn at time of diagnosis and 2 years after diagnosis.[67]

Among active duty servicemembers, there is a high prevalence of families with multiple generations of military service. A 2011 Pew Research study found 79% of veterans have an immediate family member who served in the military.[68] A report by Defense Human Resources Activity on military recruits from October 2012-March 2013 found over 25% of recruits had a parent who had served in the military and 81% had at least one family member (parent, sibling, grandparent, aunt/uncle or cousin).[69] With the high prevalence of multigenerational military service in families, there is a high chance the sera of multiple family members have already been collected. This immense repository, the largest of its kind in the world, has the capability to not only perform familial cascade testing but also streamline future genetic and genomic studies by eliminating time for sample collection.

Conclusions

The 2019 Consensus is instrumental in guiding prostate cancer germline testing. Its expanded testing indications have major implications to the MHS in increasing the number of patients testing and guiding clinicians in treatment, active surveillance, screening discussions, and the identification of hereditary cancer syndromes. The prioritization by the 2019 Consensus for more research on the characterization of genetic predisposition to prostate cancer in racially diverse populations is a promising step in addressing this issue at the national level. Studies of the African American population within the MHS have begun to better understand the genetic predisposition and disease progression of African Americans to prostate cancer, and the MHS has the ability and access to care to implement germline testing for a larger patient cohort and provide appropriate care.

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Special note

We dedicate this article to the memory of Colonel (Ret) David G. McLeod, MD, JD, the legendary soldier, doctor, and leader in Military Medicine.[70] □

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