The National Comprehensive Cancer Network now recommends *BRCA1/2* genetic testing in men with metastatic prostate cancer. The purpose of this article is to provide a review of principles of genetic testing in prostate cancer and highlight the significance of clinical genetic testing of *BRCA1/2* and other genes (*CHEK2*, *HOXB13*, *PALB2*), including Lynch syndrome genes (*MLH1*, *MSH2*, *MSH6*, and *PMS2*) in men with metastatic prostate cancer. The potential impact of genetic testing on systemic treatments and the significance of the pathogenic results for at-risk family members is discussed.

AT A GLANCE

- *BRCA1/2* genetic testing is indicated for men with metastatic prostate cancer, regardless of age or family history.
- Genetic testing results for *BRCA1/2* and other cancer susceptibility genes affect treatment options and recommendations for cancer prevention and detection in men with metastatic prostate cancer.
- Identification of a genetic mutation has implications for at-risk family members and provides opportunities for cancer screening and prevention.

KEYWORDS
metastatic prostate cancer; genetic testing; Lynch syndrome; *BRCA1/2*

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Metastatic Prostate Cancer

Effects of genetic testing on care

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Increased understanding of genetic predisposition to developing prostate cancer is directly influencing the treatment of prostate cancer. In late 2017, the National Comprehensive Cancer Network (NCCN) released updated guidelines that, for the first time, recommended *BRCA1*/2 genetic testing in men with metastatic prostate cancer (Daly et al., 2017). This article aims to highlight the significance of clinical genetic testing of *BRCA1*/2 and other genes in men with metastatic prostate cancer.

Prostate Cancer

Prostate cancer is the most common cancer in men in the United States, and about one in nine men will be diagnosed with prostate cancer during his lifetime. An estimated 164,690 men were diagnosed with the disease in 2018, and about 29,430 died from it that same year (American Cancer Society, 2018). Multiple local and systemic treatment options are available for prostate cancer. Local therapies include surgical resection and/or radiation therapy via external beam radiation therapy, brachytherapy, or radioactive seed implants. A wide variety of systemic treatment options are available and include hormone-based therapy, chemotherapy, immunotherapy, and personalized targeted treatments (NCCN, 2018c).

Screening for prostate cancer is controversial. Multiple screening modalities are available for prostate cancer, including digital rectal examination, serum testing of prostate-specific antigen (PSA), and imaging (e.g., ultrasound, magnetic resonance imaging) (NCCN, 2018d). In 2018, the U.S. Preventive Services Task Force ([USPSTF], 2018a) released updated guidelines recommending a personalized approach for prostate cancer screening after issuing a grade D recommendation (recommend against screening because the harms may be greater than the benefits) for PSA-based prostate cancer screening for men in the United States, regardless of age, in 2012 (Moyer, 2012; USPSTF, 2018b). Retrospective research has demonstrated that metastatic prostate cancer rates were steadily declining from 2004–2007 by 1.45% per year but began to increase by 0.58% per year after 2008 and further accelerated to 2.74% per year following the 2012 USPSTF recommendations not to screen for prostate cancer (Kelly, Anderson, Rosenberg, & Cook, 2018). It remains to be seen whether the USPSTF change in guidelines related to prostate cancer screening will affect rates of newly diagnosed and metastatic prostate cancer.

Metastatic Prostate Cancer

Among men who develop metastatic prostate cancer, a paradigm shift has occurred in terms of national guidelines recommending *BRCA1*/2 genetic testing (NCCN, 2018a). To qualify for a personalized hereditary cancer risk assessment and *BRCA1*/2 genetic testing, a man with metastatic prostate cancer must meet at least one of the following conditions: (a) have undergone biopsy proving metastatic disease; (b) have radiologic evidence of distant metastatic disease, such as