# Men & BRCA: A Q&A with Susan Domchek, MD

There is a common misconception that *BRCA1* and *BRCA2* mutations, also known as pathogenic variants, only impact women due to the association with increased breast and ovarian cancer risk. Men with either a *BRCA1* or *BRCA2* gene mutation also have a heightened chance for certain cancers, including male breast cancer, prostate cancer, pancreatic cancer, and melanoma. These gene mutations can be passed on to male and female children by either parent.

1. **What and when should we be telling our sons about genetic testing recommendations, screenings, and preventative options?**

   Men should consider genetic counseling and testing for *BRCA1* or *BRCA2* mutations if:

   - There is a known history of a BRCA mutation in the family.
   - There is a known history of male breast cancer, prostate or pancreatic cancer in the family.
   - There is a history of early breast cancer (under age 50) and/or a history of ovarian cancer in close female relatives.
   - The family is of Ashkenazi Jewish ancestry (Central and Eastern Europe).

   If you are considering genetic testing, it is important to consult with a genetic counselor or other healthcare provider to discuss the risks and benefits of genetic testing. *Find a genetic counselor in your area via* (https://findageneticcounselor.nsgc.org/)

   A personalized cancer risk management program can be developed for individuals who have hereditary cancer risk, such as due to *BRCA1* or *BRCA2* gene mutations. You and your healthcare providers will determine what plan makes the most sense for you.

   Cancer risk management for men with *BRCA1* or *BRCA2* gene mutations typically includes annual clinical breast exams by a physician starting at age 35 and consideration of prostate cancer screening (particularly for those with *BRCA2* mutations) starting at age 40. Additionally, some men choose to pursue BRCA genetic testing before age 35 for family planning information.

2. **What are the current recommendations for prostate cancer screenings? For pancreatic cancer screenings?**

   The average man has a 16% chance of developing prostate cancer, while *BRCA2* mutation carriers have an increased risk up to 25%, and these cancers can be more aggressive, meaning they need treatment as opposed to a “watch and wait” approach. Men with *BRCA1* mutations may also develop prostate cancer at a younger age than men in the general population. At age 40, prostate cancer screenings are recommended for *BRCA2* mutation carriers and can be considered for *BRCA1* mutation carriers. Prostate cancer screenings may include prostate-specific antigen (PSA) blood tests and digital rectal exams.

The average man has a 1% chance of developing pancreatic cancer, while *BRCA1* mutation carriers have an approximately 2-3% lifetime risk and *BRCA2* mutation carriers have an approximately 3-5% lifetime risk. There is some limited data about the effectiveness and sensitivity of pancreatic cancer screening, particularly among people who have a family history of pancreatic cancer, and this is an area of ongoing research. Pancreatic cancer screening may be considered for individuals with a *BRCA1/2* gene mutation starting at age 50 (or ten years prior to the youngest diagnosis in the family) and may occur through endoscopic ultrasound (EUS) or abdominal magnetic resonance imaging (MRI). If possible, pancreatic cancer screening should occur at an experienced, high-volume medical center. Individuals with *BRCA1/2* gene mutations who are considering pancreatic cancer screening should speak with their physicians about the potential benefits, risks and limitations.

**3. What advancements have been made in treating prostate cancer?**

The Basser Center continues to study how to optimize therapies for patients with BRCA-related prostate cancer, including clinical trial research focused on PARP inhibitors in combination with other therapies to create even more targeted and effective treatment options for patients. Polymerase (PARP) repairs DNA damage in cancer cells, allowing these malignant cells to continue to divide. PARP inhibitors work to slow tumor growth in cancers related to *BRCA1* and *BRCA2* mutations. This work at the Basser Center for BRCA includes:

**PLATPARP**, an investigator-initiated phase II trial led by Dr. Narayan, will further investigate the optimal role of PARP inhibitors for treatment of prostate cancer. This study is designed to evaluate the initial safety and effectiveness of an investigational drug, niraparib, given to patients who have recently received platinum-based chemotherapy for the treatment of prostate cancer. The ultimate goal is so investigate whether platinum chemotherapy and PARP inhibitors can be used sequentially to improve their effectiveness.

**AMPLITUDE**, an industry-sponsored, phase 3 randomized trial led by Dr. Narayan at Penn, is evaluating the safety and efficacy of niraparib and abiraterone acetate (AA), plus prednisone compared with AA plus prednisone in patients with deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-sensitive prostate cancer (mCSPC). The primary hypothesis is that niraparib and AA, plus prednisone will improve radiographic progression-free survival (rPFS) compared with AA plus prednisone.

**4. Who should consider preimplantation genetic testing (PGT) and when? What is the process of undergoing PGT?**

Preimplantation genetic testing (PGT) is a reproductive technology that may be an option for individuals who wish to minimize the chance of passing a known gene mutation to a child. This procedure is used in combination with in vitro fertilization (IVF) to test embryos (fertilized eggs) for a specific gene mutation, such as *BRCA1* or *BRCA2* mutations. PGT insurance coverage can vary greatly depending on one's insurance plan. Those who are

interested in PGT may discuss the option in greater detail with their genetics providers and may be referred to a fertility clinic specializing in this service for more information.

5. **What is the male breast cancer risk for BRCA mutation carriers and what screening options are recommended?**

   The average man has a 0.1% breast cancer risk, while male *BRCA1* mutation carriers have a 1-5% lifetime risk and male *BRCA2* carriers have a 5-10% lifetime risk. Typically starting at age 35-40, male BRCA carriers should begin self-breast exams and undergo clinical breast exams every 12 months with a physician. A mammogram will be discussed as an option on an individual basis. Mammograms are done the same way in men as they are in women. A mammogram is a low-dose X-ray procedure that produces images of the inside of the breasts. Mammography can detect some suspicious breast changes that are too small or too deep to be felt on breast examination.