

## Management Recommendations and Risk Reduction Options for Transgender Men with *BRCA1* or *BRCA2* Mutations

### Terminology

- Cisgender man/male: An individual who was assigned male at birth and identifies as male.
- Cisgender woman/female: An individual who was assigned female at birth and identifies as female.
- Transgender man/male: An individual who was assigned female at birth but their gender identity is male.

The available data suggests that individuals with breasts and ovaries who have mutations in the *BRCA1* and *BRCA2* genes have between a 50-75% lifetime risk to develop breast cancer and a 15-60% lifetime risk to develop ovarian cancer (this includes cancer of the fallopian tubes and the peritoneum, or the membrane covering the organs in the abdomen) by the time they are 70 years of age. These figures are significantly higher than the 12-13% lifetime risk for breast cancer and the 1-2% lifetime risk for ovarian cancer in the general population. Individuals with *BRCA1/2* gene mutations also have a greater chance of developing a second new primary breast cancer in the remaining breast tissue (as high as ~20-60% lifetime risk).

### Breast Cancer Screening and Risk-reduction options

Several types of surgical procedures are available for individuals identifying as male who desire chest reconstruction, also known as female to male (FtM) chest surgery and sometimes referred to as “top surgery”. Surgeons may choose the procedure based on the breast size and the individual’s personal preference.

### Breast Cancer Risk Management Options for Individuals with Breast Tissue and a *BRCA1/2* Mutation

Screening	Risk Reduction	Prophylactic Surgery
<ul style="list-style-type: none"> <li>•Ages 25-29: Yearly breast MRI screening (preferred) or mammography if MRI is unavailable and clinical breast exams every 6-12 months by a breast specialist</li> <li>•Ages 30-75: Yearly mammogram and yearly Breast MRI (spaced around the calendar year such that they are scheduled six months apart)</li> <li>•Clinical Breast exam every 6-12 months (consider one by a breast specialist and one by a gynecologist or primary care physician)</li> </ul>	<ul style="list-style-type: none"> <li>•Medications such as Tamoxifen or Evista (raloxifene) have been shown to reduce the risk of future breast cancer in individuals at increased risk of the disease.</li> <li>•We do not have a lot of data on how these medications will affect risk in individuals with <i>BRCA</i> mutations, but expect more data to be available in the future.</li> <li>•Taking tamoxifen following a diagnosis of an estrogen-receptor negative (ER-) tumor is somewhat controversial; please speak to your physicians about the pros and cons of taking tamoxifen.</li> </ul>	<ul style="list-style-type: none"> <li>•Bilateral prophylactic mastectomy (removal of healthy breast tissue before a cancer diagnosis) has been shown to reduce the risk of a future breast cancer diagnosis in individuals with <i>BRCA</i> mutations by &gt;90%</li> </ul>

**Individuals with a BRCA1/2 mutation who have had FtM chest surgery, or “top surgery”**

- The FtM chest surgery, sometimes referred to as “top surgery”, reduces the risk of developing breast cancer, however there may be residual breast tissue in the chest wall after top surgery which remains at risk of breast cancer. Top surgery does not decrease breast cancer risk as much as a risk-reducing mastectomy, as the procedures differ in the way they are completed.
- Mammography screening or breast MRIs may not always be possible following FtM top surgery due to a lack of breast tissue, however an annual clinical chest exam with a breast cancer specialist is necessary. It is important to discuss your personalized risk and screening recommendations with your physicians based on the residual breast tissue.

**Individuals interested in prophylactic risk-reducing bilateral mastectomy**

- Given the limitations of top surgery with respect to breast cancer risk-reduction, patients considering top surgery may opt for a mastectomy, rather than top surgery that leaves some breast tissue in place. Prophylactic mastectomy has been shown to reduce the risk of a future breast cancer diagnosis in individuals with BRCA1/2 mutations by >90%

**Ovarian Cancer Screening and Risk Reduction Options for Individuals with Ovaries and Fallopian Tubes and a BRCA1/2 Mutation**

Screening and Prophylactic Surgery	Risk Reduction
<ul style="list-style-type: none"> <li>• Risk reduction options and prophylactic surgery are preferred as data do not support routine ovarian cancer screening. The current screening techniques for ovarian cancer have not been shown to detect ovarian cancer at an early, more treatable stage.</li> <li>• For individuals who choose to not have prophylactic surgery, screening options beginning at age 30-35 include transvaginal doppler ultrasound and CA125 blood marker screening every 6 months.</li> </ul>	<ul style="list-style-type: none"> <li>• Use of oral contraceptives (birth control pills) can reduce the overall lifetime risk of ovarian cancer. Several studies now show that this risk reduction can also be seen in individuals who carry <i>BRCA</i> mutations.</li> <li>• Taking oral contraceptives following a diagnosis of breast cancer is often contraindicated; if you have had breast cancer, please speak to your physicians about the appropriateness of taking oral contraceptives.</li> </ul>

Transgender men do not always have ovaries and fallopian tubes removed as part of their transition. However, it would be recommended to have both the fallopian tubes and ovaries removed between the age of 35 and 45, given the increased risk for ovarian cancer with a BRCA1/2 mutation.

## Family Planning, Reproductive Options, and Reproductive Risks

### **Fanconi Anemia and BRCA2 mutation**

Rarely, a child can inherit two *BRCA2* mutations, one from each parent. This causes a different hereditary syndrome known as Fanconi Anemia. Children with Fanconi Anemia are at increased risk to develop bone marrow failure, leukemia, and other cancers, as well as physical differences such as changes in the thumb, small skull size, and short stature. For this reason, individuals with a *BRCA2* mutation who are of reproductive age may wish to consider having their partners tested for mutations in the *BRCA2* gene before becoming pregnant. If both parents have a *BRCA2* mutation, then there is a 25% risk their children will have Fanconi Anemia. We would be happy to coordinate testing through our office or provide information about genetic clinics in their area.

### **Egg Preservation**

Decisions about family planning (i.e. whether, how and when to have children) are personal to everyone, regardless of whether or not they have a genetic condition. Some individuals with a *BRCA1/2* mutation who are interested in having children using their eggs may want to pursue family planning options that can prevent the mutation from being passed to their children. Individuals planning to have their ovaries and/ or fallopian tubes removed based on the recommendations and/ or as a part of the FtM transition may want to pursue ovarian tissue preservation or egg preservation. If or when embryos are created, *BRCA1/2* testing through pre-implantation genetic diagnosis (PGD) can be considered.

### **Hormone exposure**

Testosterone therapy is an important part of transition for some individuals. There is limited research regarding the risk of breast cancer in transgender men with *BRCA1/2* mutations using hormone therapy. It is known that testosterone in the body can be converted to another hormone, called estrogen. However, the role of supplemental testosterone in breast cancer development is still unclear at this time. A consultation with an oncologist should be considered prior to hormone use.