alex ooi & associates
OBGYN CONSULTANTS

3 Mount Elizabeth #11-07
Mount Elizabeth Medical Centre
Singapore 228510

T +65-6738 8331
F +65-6734 8896
dralexooistaff@gmail.com
www.obgyndr.org
Obgyn Consultants Pte Ltd

Genetic Testing for BRCA1 and BRCA2

Genetic testing gives the chance to learn of family history of breast cancer being due to an inherited gene mutation. Most women who get breast cancer do not have an inherited gene mutation. Five to 10 percent of breast cancers in the U.S. are linked to an inherited gene mutation.

Every cell in your body contains genes. Genes contain the blueprints (genetic code) for your body. For example, they contain the information that determines the color of your eyes. They also contain information that affects how the cells in your body grow, divide and die.

The information in your genes is passed on (inherited) from both your mother and your father. And, you can pass this information on to your children, both your daughters and sons.

Some changes in the genetic code that affect the function of the gene are called mutations. Mutations are rare. However, just as with other information in genes, mutations can be passed on from a parent to a child.

Some inherited gene mutations increase breast cancer risk. *BRCA1* and *BRCA2* (BReast CAncer genes 1 and 2) are the best-known genes linked to breast cancer. People who have a *BRCA1* or *BRCA2* mutation have a greatly increased risk of breast cancer and (for women) ovarian cancer. However, there are some.

Who should consider testing?

Genetic testing for *BRCA1* and *BRCA2* is recommended for certain people, including those with:

- A known *BRCA1/2* gene mutation in the family
- A personal history of breast cancer at age 45 or younger
- A personal history of breast cancer at age 50 or younger and a family member (parent, sibling, child, grandparent, grandchild, uncle, aunt, nephew, niece or first cousin) diagnosed with breast cancer at any age
- A personal history of triple negative breast cancer (breast cancer that is estrogen receptor-negative, progesterone receptor-negative and HER2/neu receptor-negative) diagnosed at age 60 or younger
- A personal history of ovarian cancer
- A personal or family history of male breast cancer
- Ashkenazi Jewish heritage and a personal or family history of breast or ovarian cancer
- A family member (parent, sibling, child, grandparent, grandchild, uncle, aunt, nephew, niece or first cousin) diagnosed with breast cancer at age 50 or younger
- A family member (parent, sibling, child, grandparent, grandchild, uncle, aunt, nephew, niece or first cousin) diagnosed with ovarian cancer at any age

There is only a very small chance that your family carries a *BRCA1/2* mutation if:

- You or an immediate family member is the only person in your family with breast cancer
- The breast cancers in your family all occurred at older ages

In most cases, genetic testing is not recommended when there is a low chance of finding a mutation. Remember, most breast cancers are not due to a *BRCA1/2* mutation. Although testing for a *BRCA1/2* gene mutation just requires a blood test, the risks and benefits should be considered before testing. There are potential physical, emotional and financial impacts of knowing your genetic status. Thus, testing for a *BRCA1/2* mutation is recommended only for people who fall into one of the categories listed above.

Talking with your health care provider

If you have concerns about your risk of having a *BRCA1/2* gene mutation, talk with your health care provider. He/she can help you understand your risk and can refer you to a genetic counselor.

There are a few online tools to help you talk with your provider about your risk of a *BRCA1/2* mutation and your risk of breast cancer. Please keep in mind these tools cannot tell you whether or not you have a *BRCA1/2* mutation or if you will get breast cancer. Rather, they may help you talk with your provider or a genetic counselor about these risks.
The Centers for Disease Control and Prevention (CDC) along with breast cancer advocacy organizations (including Susan G. Komen) created an online tool called *Know:* BRCA. This tool can help younger women assess their risk of a *BRCA1/2* mutation. This information can help you talk with your provider or a genetic counselor about your risk of a *BRCA1/2* mutation.
The Office of the Surgeon General and the National Human Genome Research Institute (part of the National Institutes of Health) created an online tool called "My Family Health Portrait" to help you create a chart of your family's health history. This chart may be useful in discussions with your provider or genetic counselor about your family history of breast cancer and/or other health conditions.

Testing for *BRCA1/2* mutations

In most cases, testing is first done on the person with breast or ovarian cancer. If no mutation is found, the cancer was probably not due to a *BRCA1/2* mutation and there is no need to test other family members. If a *BRCA1/2* mutation is found, other family members can be tested for the specific mutation. It is not likely that all family members will have the mutation. For example, if your mother has a *BRCA1* or *BRCA2* mutation, there is only a 50 percent chance that you will also have a mutation (you get half of your genes from your mother and half from your father).
If your family members with breast cancer or ovarian cancer are deceased or are not willing to be tested (or if your family medical history is unknown), a genetic counselor can help you decide whether it would be useful for you to have *BRCA1/2* testing.

Testing for other gene mutations

Of the genes linked with breast cancer, *BRCA1* and *BRCA2* are the most well-understood. When a person is found to have a mutation in one of these genes, there are special recommendations for breast cancer screening, risk-lowering options and care. So, genetic testing for *BRCA1/2* mutations can affect a person's medical care.
Inherited gene mutations in some other genes such as *p53*, *CHEK2*, *ATM* and *PALB2*, also increase breast cancer risk. Testing for some of these mutations exists. However, these gene mutations are rare and little is known about how to tailor medical care to people with these mutations. So, although testing for multiple gene mutations is becoming more available, health care providers do not yet know how to use much of the information from these tests.
If your family members with breast cancer or ovarian cancer are deceased or are not willing to be tested (or if your family medical history is unknown), a genetic counselor can help you decide whether it would be useful for you to have testing for other inherited gene mutations.

At-home genetic testing

You may have seen ads for at-home genetic testing kits. These kits are not recommended for assessing breast cancer risk. The U.S. Food and Drug Administration, U.S. Federal Trade Commission and Centers for Disease Control and Prevention all caution against the use of at-home testing kits. The results of any genetic test should be interpreted by a trained health care provider or genetic counselor [261-263].

BRCA1/2 genetic test results

Results from a *BRCA1/2* test show whether there is a mutation related to cancer in either the *BRCA1* or *BRCA2* gene. There are three possible results:

- No mutation (negative or normal)
- A mutation linked to cancer (positive or carrier)
- A mutation not currently known to increase breast cancer risk (called a variant of uncertain significance)

Having a *BRCA1/2* mutation does not mean you will get breast cancer. Some people with a mutation will never get breast cancer. And, people without a mutation are still at risk. Most women who develop breast cancer do not have a *BRCA1/2* mutation [4]. If you have a *BRCA1/2* mutation, there are some options to help lower your risk of breast cancer. You should discuss these options with your health care provider.
Learn more about how to reduce your risk of breast cancer at healthy lifestyle and breast cancer risk.

Benefits of *BRCA1/2* genetic testing

Emotional benefits

For some people, learning their genetic test results (even if a *BRCA1/2* mutation is found) brings a sense of relief and empowerment. Some may even find that learning they have a *BRCA1/2* mutation is less stressful than wondering whether they have one. There is hope of benefit from the risk-lowering options available today.
Testing negative can bring a sense of relief about the risk of breast and ovarian cancer for you and for your children.

Options for *BRCA1/2* carriers to lower their risk of breast cancer

- Taking a risk-lowering drug (tamoxifen or raloxifene)
- Having a prophylactic mastectomy
- Having a prophylactic oophorectomy

If you are a carrier, talk to your health care provider.

Breast cancer screening for *BRCA1/2* carriers

Knowing you have a *BRCA1/2* mutation allows you to personalize your breast cancer screening plan. For example, women with a *BRCA1/2* mutation are screened more often and start screening at a younger age than other women. Screening with breast MRI in combination with mammography is also recommended. Mammography plus breast MRI is better than mammography alone at finding breast cancer. No matter the result, do follow screening guidelines.

Screening and risk-lowering options for ovarian cancer

Women who have a *BRCA1/2* mutation also have a higher risk of ovarian cancer. These women may consider prevention options (such as prophylactic oophorectomy) to reduce the risk of ovarian cancer.
At this time, screening methods to detect early stage ovarian cancer are still under study.

Benefits for family members

Getting genetic testing lets you share your test results with family members who may benefit from having the option of genetic testing. Remember, not every family member will have the mutation.

Risks of *BRCA1/2* genetic testing

Psychological/emotional risks

If you are thinking about having *BRCA1/2* testing, consider the emotional impact of the test results. For some people, knowing they have a *BRCA1/2* mutation causes worry and anxiety even though they may never get breast cancer. Some people may feel overwhelmed when faced with the medical options that can lower their risk.
People who test positive for a *BRCA1/2* mutation are encouraged to share this information with their family members who may be at risk. This can be a difficult task. A parent who tests positive may find dealing with the possibility that his/her child is at risk harder than dealing with his/her own risk.
Getting a negative *BRCA1/2* test result is usually seen as good news. However, this news can also cause awkward feelings around relatives who have had cancer or who test positive for a *BRCA1/2* mutation. And for some, knowing they do not have a mutation may give a false sense of security of not being at risk of breast cancer.
Getting a result of a variant of uncertain significance (and not knowing whether the mutation increases risk) can be confusing or frustrating and may add to the stress of an already trying process.
If your *BRCA1/2* test results (or even the option of genetic testing) upset you, talk to your health care provider. It may also be helpful to discuss these issues with a mental health provider, such as a therapist or a psychologist.
Connecting with other people who have had *BRCA1/2* testing may also help.

Prepared for your basic information by:
DR ALEX K H OOI, PKT, DJN
MBBS, MMED(O&G), FAMS, FRCOG, FICS, MBA