National Cancer Centre Singapore
SingHealth

Inspired By Hope, Committed to Care

A GUIDE TO GENETIC TESTING FOR

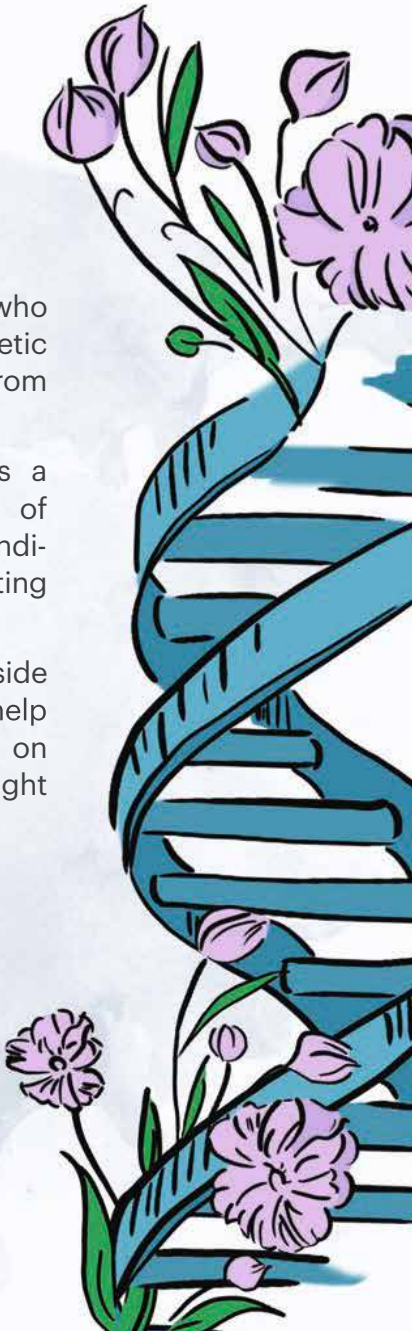
HEREDITARY BREAST & OVARIAN CANCER

About this booklet

It is important that individuals who are considering cancer genetic testing seek medical advice from a health professional.

This booklet was created as a guide outlining the basics of hereditary cancer and the conditions under which genetic testing may be useful.

Please use this booklet alongside qualified medical advice, to help make an informed decision on whether genetic testing is right for you.



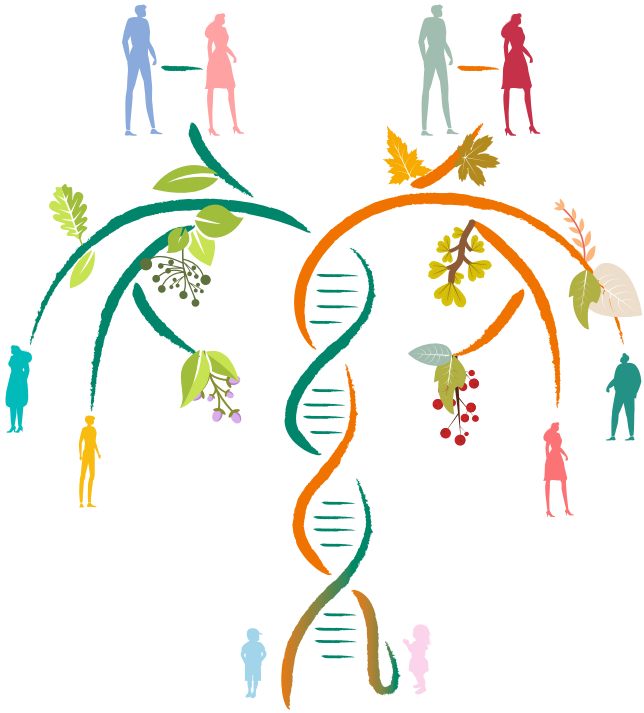
What is hereditary cancer?

HEREDITARY CANCERS make up about 5-10% of all cases of cancer.[1] Some genes function to protect us from cancer; when they are not working well, it causes hereditary cancer. We will refer to genes that are not working well as faulty genes.

Individuals who carry a faulty gene(s) have a higher chance of developing certain cancers compared to the general population. The types of cancers that they may be at increased risk for will depend on the gene(s) involved.

Not all family members will inherit the faulty gene(s), and genetic testing can be done to verify this.

Additionally, not everyone who inherits a faulty gene(s) will develop cancer.



What are the different forms of cancer and how do they develop?

HEREDITARY CANCERS

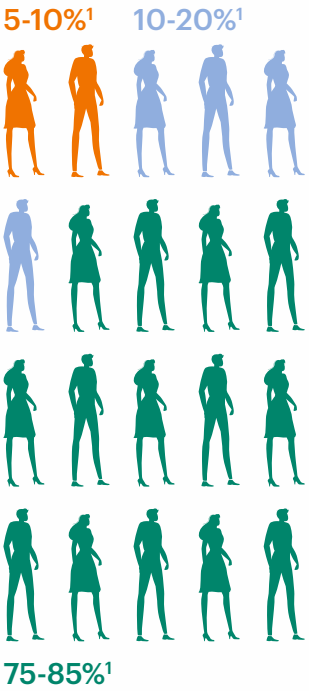
Caused by **one or more faulty gene(s)** that run in the family, and usually develop at younger ages.

FAMILIAL CANCERS

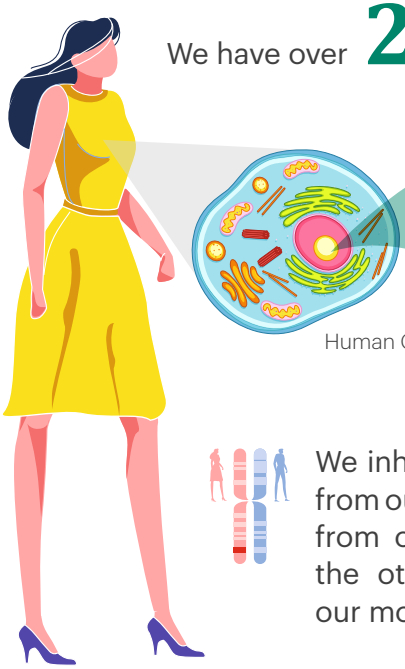
Caused by a combination of certain genes, that interacts with an individual's environment and lifestyle factors to raise his/her risk of cancer.

SPORADIC CANCERS

Caused by chance events; **age and environmental factors** are generally the biggest factors increasing the risk of such cancers.

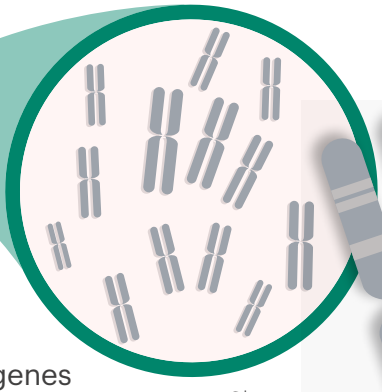


What are genes?



We have over **25,000** genes in our body.

Human Cell

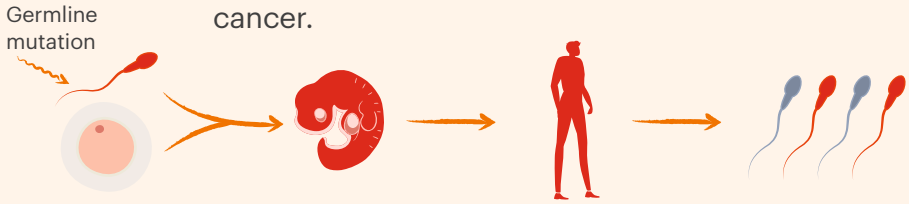


Chromosome

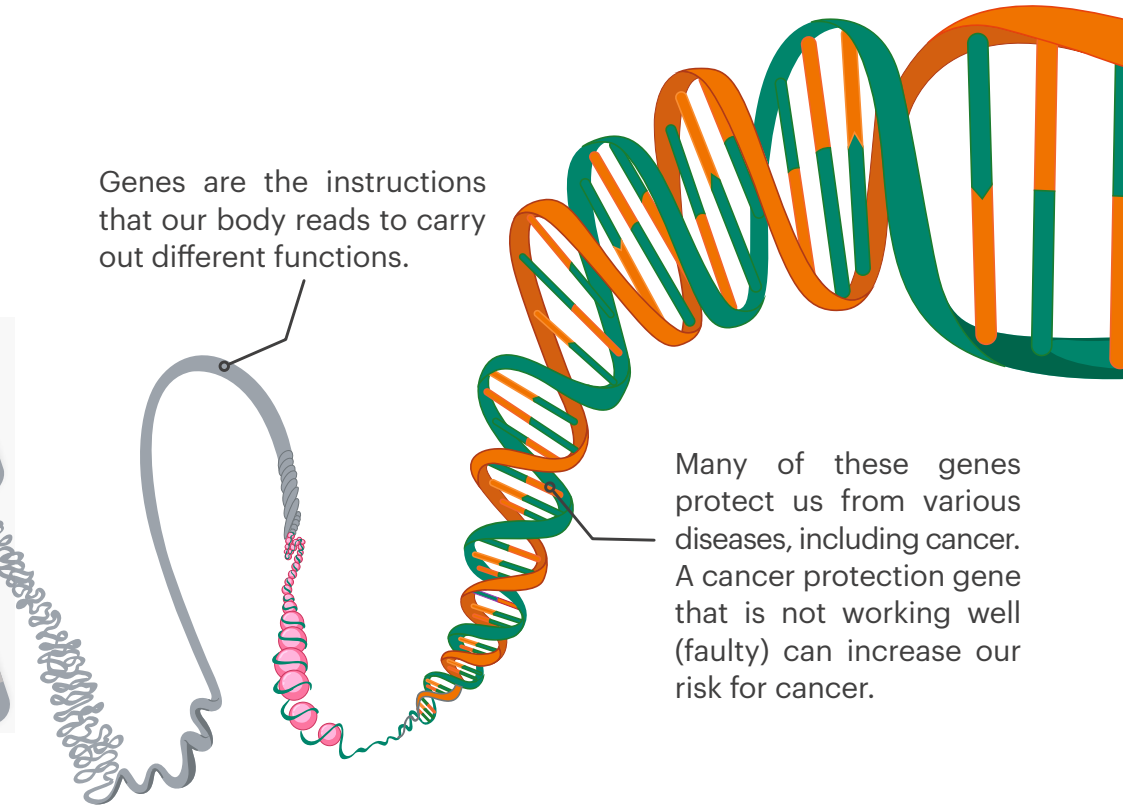
We inherit our genes from our parents, half from our father and the other half from our mother.

There are two kinds of gene faults (mutations), namely

GERMLINE MUTATIONS are usually inherited from a parent and can be passed down to children. They are found in all the cells of an individual. This is what drives hereditary cancer.



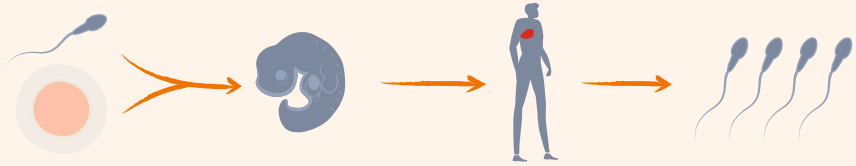
Genes are the instructions that our body reads to carry out different functions.



Many of these genes protect us from various diseases, including cancer. A cancer protection gene that is not working well (faulty) can increase our risk for cancer.

y GERMLINE and SOMATIC:

SOMATIC MUTATIONS are acquired as you age. They are not inherited from parents or passed down to children. They are present only in cancer cells but absent from non-cancer cells. This is what drives sporadic cancer.



Parental sex cells without mutation

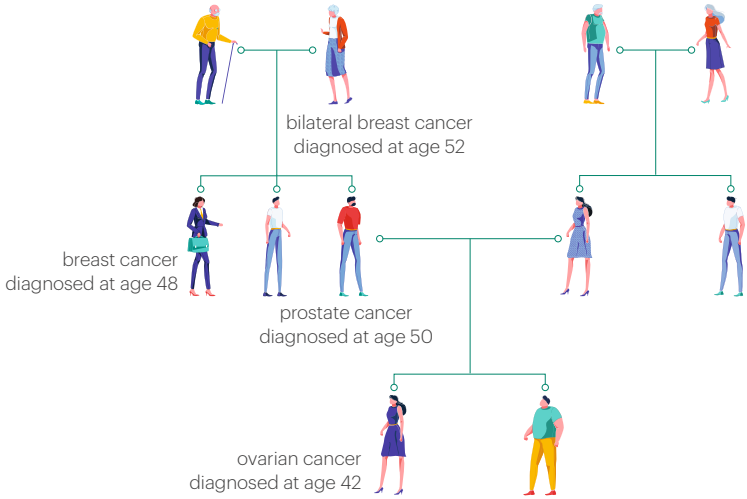
Embryo (without mutation)

Individual acquires mutations in some cells of their body with age

Mutation is not passed down to children, as it is not carried by sex cells

When is hereditary cancer suspected?

- A strong family history of cancer: Multiple individuals diagnosed with similar types or patterns of cancer on either side (paternal/maternal) of the family.



- Young age of cancer diagnosis: Individuals who are diagnosed with cancer at a younger age.
- Multiple cancers: Individuals who are diagnosed with more than one primary cancer over their lifetime.
- Rare tumours or cancers: unusual tumours (e.g. neuroendocrine tumours) or cancers (e.g. sarcoma).

However, in some cases a family history of cancer may be 'hidden' by factors such as:

- adoption/lack of genealogical information
- small family structure
- male-dominant family
- family members who carry a faulty gene(s) but do not develop cancer

Hence, in some cases, genetic testing is offered even in the absence of a family history of cancer.

What are the benefits of knowing your genetic test result?

FOR YOURSELF

Your genetic test result may help you:

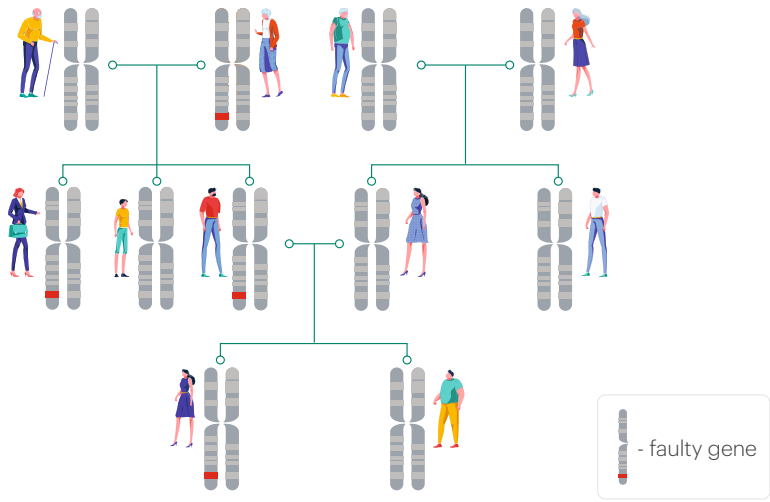
- determine if you are at increased risk of cancer, and what these types of cancers are.
- receive personalised recommendations from your healthcare professionals on how to reduce your specific cancer risks.
- better decide on cancer treatment options (certain hereditary cancers respond well to specific drugs, such as PARP inhibitors).

FOR YOUR FAMILY

Your genetic test result may help:

clarify whether hereditary cancer runs within your family

If you carry a faulty gene(s), this would indicate that your family members are at risk of carrying the same faulty gene(s).

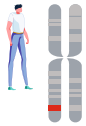


As such, your family members (parents, siblings, children and extended relatives) should:

consider undergoing genetic testing to check if they have also inherited the faulty gene(s) and have an increased risk of cancer

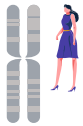
However, not all family members who inherit the faulty gene(s) will develop cancer.

Family members who inherit the faulty gene(s):



- will be offered cancer screening strategies to detect the presence of cancer at an early and manageable stage
- can consider risk-reducing surgery to lower their risk of cancer

Family members who do not inherit the faulty gene(s):



- can be reassured that their risk of developing cancer is similar to that of the general population
- can avoid unnecessary screening and medical costs
- can be reassured that their children are not at risk of inheriting the faulty gene(s)

How is genetic testing done?

Genetic testing typically is a **one-time blood test.** If a blood sample cannot be taken, other sample sources (e.g. skin or saliva) may be explored.

Blood

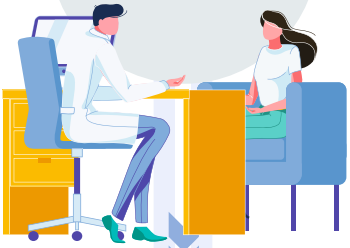
Saliva

Skin

What is the process of genetic counselling and testing?

01

Pre-test genetic counselling



Before genetic testing is conducted, a consultation (~30mins) will be arranged with a genetic counsellor and/or a medical oncologist to discuss the following:

- Personal and family history of cancer and/or disease
- Assessment of how likely a hereditary cause is the reason for the cancer(s) in the family and whether genetic testing is recommended
- Benefits and limitations of genetic testing personalised for you and your family
- Implications of the genetic test result on insurance, legal and privacy issues

02

Consent for genetic testing obtained

Genetic testing is a personal choice and no one is forced to go ahead with it. You need to consent to genetic testing before it is conducted.

04 Result appointment

Your result appointment will involve a discussion of the following aspects of your genetic test result:

- What this result means for you and your family
- Whether anyone else in the family should also consider genetic testing
- Personalised recommendations on how to manage and reduce your cancer risks based on your result and your family history of cancer (if any)
- Referrals to other specialities (if needed) to facilitate the cancer risk management plan recommended to you
- Support for you and your family members

03 Collection of samples

A blood (sometimes skin or saliva) sample will be taken for genetic testing.

Most genetic test results are ready in 2–6 weeks. As such, the clinic will schedule an appointment to discuss your test result with you after that period.

What are the possible results from genetic testing?

There are 3 types of results you may receive:

Positive

Faulty gene(s) identified

Uncertain

Variant of Uncertain Significance (VUS)

Uncertain gene change(s) identified, unclear if these change(s) increase risk for cancer

Negative

No faulty gene(s) identified

Increased risk of developing certain cancers (type of cancer depends on faulty gene(s) involved)

Your family (parents, siblings, children and extended relatives) may have inherited the faulty gene(s) and should consider genetic testing to clarify this

May be clarified by testing other family members

May be reclassified over time as 'positive' or 'negative' when more information is known

Cancer risk is similar to that of general population

Test limitations will be explained in the context of your personal and family history of cancer

What is Hereditary Breast and Ovarian Cancer (HBOC) syndrome?

Hereditary Breast and Ovarian Cancer (HBOC) is an adult-onset hereditary cancer syndrome associated with an increased cancer risk that runs in the family.

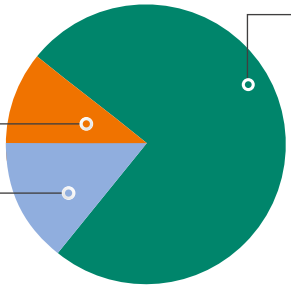
Approximately 5-15% of breast cancer is caused by a hereditary reason[2,3]

5-15%
Hereditary

Faulty *BRCA1/2* genes explain 25-50% of hereditary breast cancer. Other breast cancer genes include *ATM, CHEK2, PALB2* and more

15-25%
Familial/Polygenic

A combination of genes and environmental factors may be involved



Breast cancer

~75%
Sporadic

Chance events; age and environmental factors are generally the biggest factors

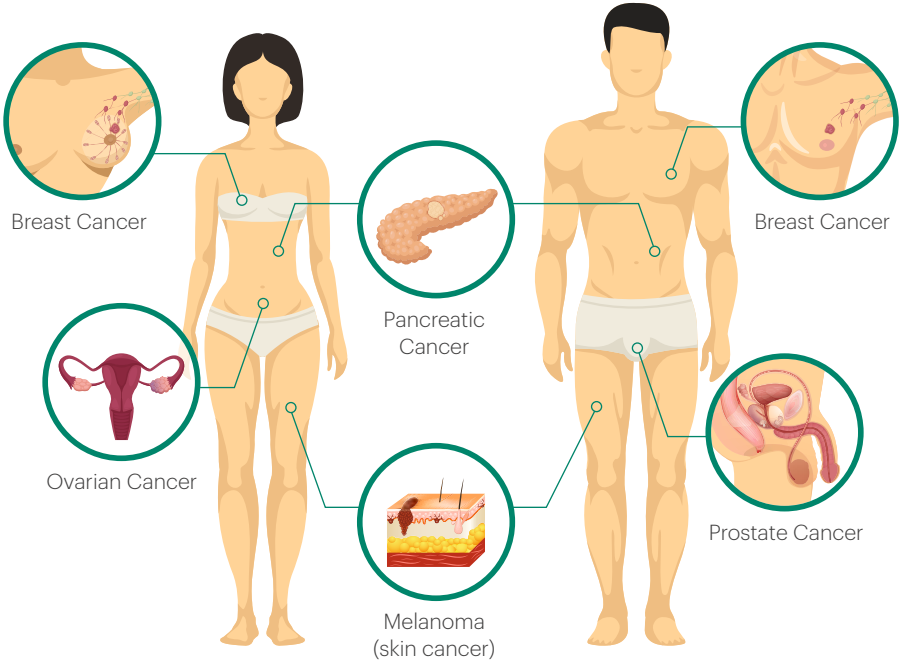
HBOC is primarily associated with a faulty *BRCA1* or *BRCA2* gene, which increases the lifetime risk of certain cancers.

Cancer type	*BRCA1*	*BRCA2*	General population
Breast	47 – 66%	40 – 57%	13%
Ovarian	35 – 46%	13 – 23%	1 – 2%
Male Breast	1.2%	~7%	0.1%
Prostate	8.6%	15%	6%
Pancreatic	May be increased	May be increased	<1%
Melanoma	Not increased	May be increased	Up to 2.6%

Table 1. Lifetime cancer risks for individuals with a faulty *BRCA1 or BRCA2* gene[4-7]

Note: The conditions associated with HBOC and its risk estimates may change as more information is available.

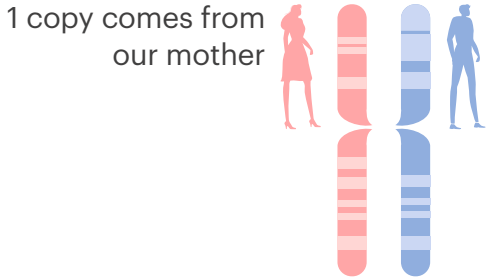
A faulty *BRCA1 or BRCA2* gene increases the risk of developing certain cancers in females and males



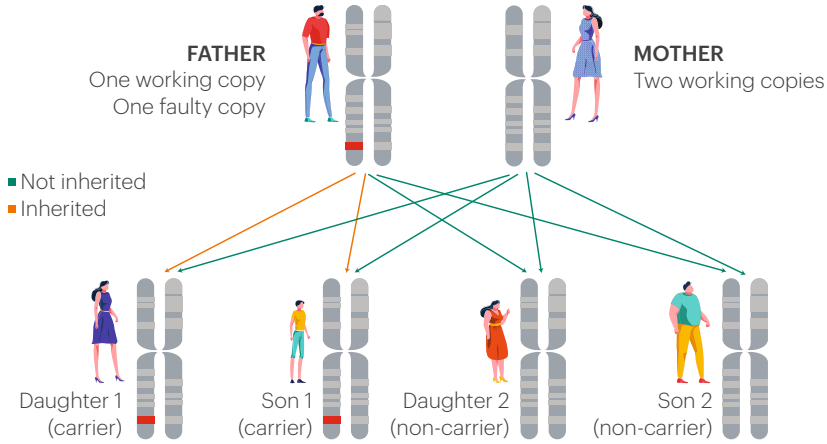
There are other genes aside from *BRCA1* and *BRCA2* associated with HBOC, they include: *ATM, BRIP1, CHEK2, PALB2, RAD50, RAD51C* and *RAD51D*. There are also genes that increase the risk of breast cancer as part of other genetic syndromes, such as: *TP53, PTEN, STK11* and *CDH1*.

How is HBOC inherited?

Everyone has 2 copies of each gene in their body's cells:



HBOC follows a dominant inheritance pattern. This means that having one faulty copy would result in an increased risk of cancer.



50% chance of passing down faulty copy of gene

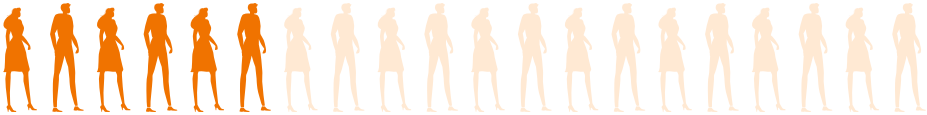
- A parent with a faulty gene(s) has a 50% chance of passing down their faulty gene(s) to their children.
- A child, sibling or parent of a family member with a faulty gene(s) has a 50% chance of also inheriting the same faulty gene(s).
- Extended relatives may also inherit the faulty gene(s).

How common is HBOC?

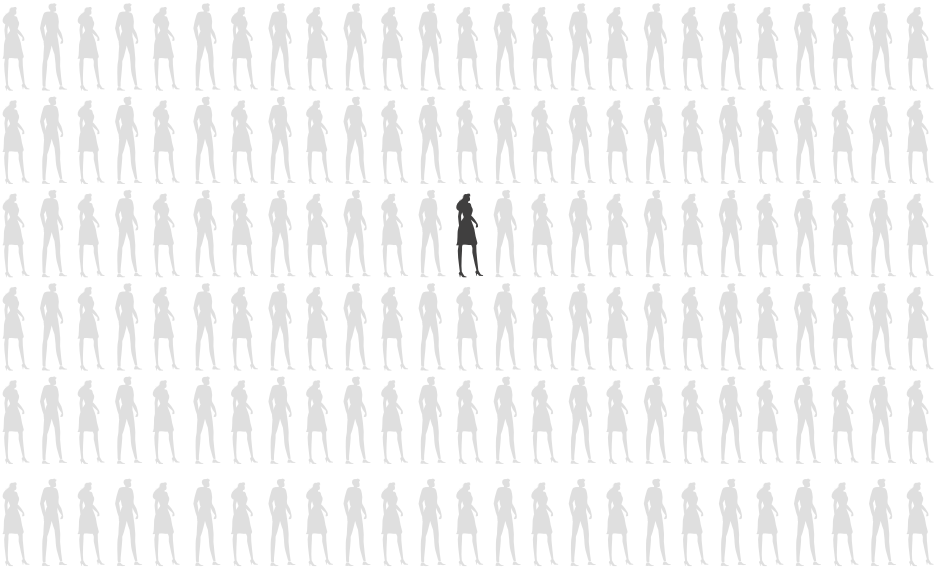
It is observed in:

5-15% of breast cancers

10-25% of ovarian cancers



Having a faulty BRCA1/2 gene may be more common than you think, a local study found roughly 1 in 150 individuals in Singapore carry a faulty BRCA1/2 gene.



Who should undergo genetic testing for HBOC?

Individuals who meet, or have family members who meet, one or more of the following criteria can consider genetic testing.

- Breast cancer diagnosed at or **under 45 years of age**
- Breast cancer diagnosed at **any age** in an individual of Ashkenazi Jewish ancestry
- Male breast cancer
- Multiple primary breast cancers either in one or both breasts
- Ovarian cancer
- Triple-negative breast cancer **before age 60 years**
- **Combination** of breast and ovarian cancer
- Pancreatic cancer
- Metastatic or high grade prostate cancer (Gleason score ≥ 7)
- Two or more relatives on the same side of a family with breast cancer, one **under age 50**
- Three or more relatives on the same side of a family with breast cancer at **any age**
- A previously identified faulty *BRCA1* or *BRCA2* gene in the family

How can your HBOC genetic test result help you?

Your genetic result may help to personalise your management options based on your cancer risk.

If you have a cancer diagnosis

- can help guide important treatment and surgery decisions
- indicates what other cancers you are at risk of and how to manage these risks

If you are currently cancer-free

- can help guide relevant screening options for you to detect cancer at its earliest, most treatable stage
- can help guide relevant cancer risk-reducing procedures (e.g. surgery)
- can help you to consider dedicated reproductive options for individuals with HBOC, if you are planning to have children

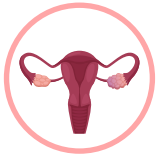
What can I do to manage my increased risk of cancer?

If you are female

SCREENING*

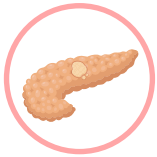
Breast cancer

- ✓ Annual mammograms and/or breast MRIs
- ✓ 6-monthly clinical breast examination
- ✓ Practice breast self-awareness



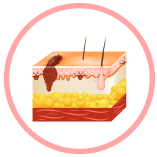
Ovarian cancer

- ◉ No effective screening method to detect ovarian cancer—risk-reducing surgery is the only recommendation.



Pancreatic cancer

- ✓ Endoscopic ultrasonography and or MRI/magnetic resonance cholangiopancreatography
- ✓ Clinical recommendations made on a case-by-case basis

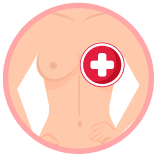


Melanoma (skin cancer)

- ✓ Annual skin check by dermatologist
- ✓ Clinical recommendations made on a case-by-case basis

*These options will be discussed in detail with you by your managing doctor(s). The age and onset for screening may depend on personal and/or family history of cancer.

RISK-REDUCING SURGERY†#



Breast cancer

- Bilateral mastectomy: surgery to remove breast tissue
- Chemo-prevention drugs (e.g. Tamoxifen) are usually offered on a case-by-case basis to reduce breast cancer risk

Ovarian cancer

- Bilateral salpingo-oophorectomy: surgery to remove ovaries and fallopian tubes

† These options will be discussed with in detail with you by your managing doctor(s).
# These surgeries reduce cancer risk significantly (~90%) but they do not remove the risk of breast or ovarian cancer completely.

LIFESTYLE ADJUSTMENTS

Pancreatic cancer

- Avoid smoking

Melanoma (skin cancer)

- Practice sun smart behavior

All cancers

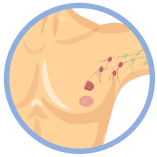
- Keep a healthy diet and active lifestyle

Note: The recommendations for screening and risk-reducing surgery may change as more information becomes available.

What can I do to manage my increased risk of cancer?

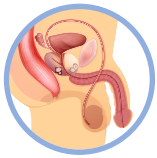
If you are male

SCREENING*



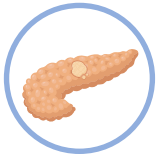
Breast cancer

- ✓ Annual clinical breast examination
- ✓ Maintenance of chest awareness and pectoral area palpation on regular basis



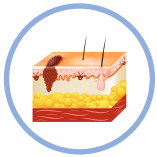
Prostate cancer

- ✓ Annual digital rectal examination (DRE)
- ✓ Annual blood test for prostate-specific antigen (PSA)



Pancreatic cancer

- ✓ Endoscopic ultrasonography and/or MRI/magnetic resonance cholangiopancreatography
- ✓ Clinical recommendations made on a case-by-case basis



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- ✓ Annual skin check by dermatologist
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LIFESTYLE ADJUSTMENTS

Pancreatic cancer

- Avoid smoking

Melanoma (skin cancer)

- Practice sun smart behavior

All cancers

- Keep a healthy diet and active lifestyle

Note: The recommendations for screening and risk-reducing surgery may change as more information becomes available.

Frequently
ASKED QUESTIONS

Who is the best person in the family to undergo genetic testing?

A

Genetic testing is recommended foremostly for the family member whose cancer diagnosis is most suggestive of a hereditary cause (e.g. young or unusual cancer). **Those with a history of cancer are more likely to have inherited a faulty gene(s) over those who do not.**

If a hereditary cause is identified, testing can be subsequently offered to at-risk relatives who do not have cancer or are asymptomatic.

In some cases, testing an affected family member is not possible and genetic testing can be offered to asymptomatic individuals.

However, there are limitations of a negative genetic test result of an asymptomatic individual:

- It may not mean that there isn't a hereditary cause for cancer in the family (i.e. the individual being tested may not have inherited it, but others in the family may have, or the faulty gene(s) may not have been identified yet)
- The result is only useful to the asymptomatic person being tested and their children, but not to their parents, siblings and other second-degree family members.

Do males need to be tested?

Genetic testing is recommended for both males and females, as both males and females can inherit faulty gene(s) that increase their risk of cancer. Faulty gene(s) can be inherited from either one's mother or father. Furthermore, males can pass down the faulty gene(s) to any of their children (sons and daughters).

Is testing recommended in children?

Genetic testing for adult-onset conditions is not recommended in children under the age of 21. Genetic testing in children is only offered when they have a personal history of certain cancers, or if the faulty gene(s) identified in the family is known to increase the risk of cancer during childhood.

Common Myths & MISCONCEPTIONS OF HBOC

If I test positive, it means my cancer will recur.

FALSE. Your genetic test result cannot determine the likelihood of cancer recurrence or the presence of cancer. A positive result only indicates an increased risk of getting cancer or of a new cancer developing.

If I test positive, it means that my children will get cancer.

FALSE. If you have a positive genetic test result, identifying a faulty gene(s), it means each of your children has a 50% (1 in 2) chance of inheriting the faulty gene(s).

My daughter looks a lot like me, so she must have inherited the faulty gene(s) since I have it.

FALSE. Genes that govern your appearance are different from cancer protection genes like *BRCA1* and *BRCA2*. All first-degree relatives (siblings, children, parents) have a 50% (1 in 2) chance of inheriting the faulty gene(s) in *BRCA1* or *BRCA2*.

I have 2 brothers, so one will inherit the faulty gene(s) and one won't, because it's 50% chance.

FALSE. Each first-degree relative (parents, siblings, children) has a 50% (1 in 2) chance of inheriting the faulty gene(s). The genetic test result of one brother does not impact the chances for the other brother.

I only have brothers, so I don't need to tell them – this can only pass through females.

FALSE. The faulty gene(s) can be passed down to and through both males and females. There are increased cancer risks to both males and females. It is therefore important for both females and males to undergo testing to understand if they have inherited the faulty gene(s).

Brothers and sisters who inherit the faulty gene(s) have a 50% (1 in 2) chance of passing it down to their children (daughters and sons).

I only need to tell my brothers, sisters and children and not my distant relatives.

FALSE. Distant relatives can inherit the faulty gene(s) (e.g. aunties, uncles, cousins). It is important to let them know so they can consider genetic testing to understand their risk of developing cancer.

Hadar T, et al. Presymptomatic Awareness of Germline Pathogenic BRCA Variants and Associated Outcomes in Women With Breast Cancer. JAMA Oncol. Published online July 09, 2020. doi:10.1001/jamaoncol.2020.2059

For more information, please refer to these resources

- **Cancer Genetics Service, National Cancer Centre Singapore (NCCS):** https://www.nccs.com.sg/patient-care/specialties-services/cancer-genetics-service
- **eVIQ:** https://www.eviq.org.au/cancer-genetics/adult
- **Cancer.net:** https://www.cancer.net/navigating-cancer-care/cancer-basics/genetics
- **FORCE:** https://www.facingourrisk.org/index.php
- **At-Risk of Cancer (ARC) Support Group:** https://www.nccs.com.sg/patient-care/specialties-services/support-groups

If you have any questions, please contact the following helplines:

Cancer Genetics Service (NCCS)

(65) 6436 8000

cgsgroup@nccs.com.sg

Cancer Helpline

(65) 6225 5655

cancerhelpline@nccs.com.sg

Alternatively, to book an appointment with the Cancer Genetics Service (NCCS), please get a referral from your doctor to speak with a genetic counsellor or medical oncologist.

Please scan the QR code to access our website.

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